Selection of Anesthesia

# Selection of Anesthesia

## THE PHYSIOLOGICAL AND PHARMACOLOGICAL BASIS

*By*

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# PREFACE

This book is not for those interested in the technique of administering anesthetics It is intended for individuals who wish to become familiar with the principles and methods of anesthesiology Emphasis is placed upon the pharmacology of the drugs used and the criteria for selecting anesthesia The book is written for physicians who are called upon to evaluate operative risks It is intended to be of interest to physicians in the surgical specialties who are responsible for prescribing anesthetic drugs and dictating methods of anesthesia but who do not themselves administer anesthetics It mav be of interest to consultants who are called upon to diagnose and advise in the management of postoperative complications The fundamental principles presented, though elementary, may also be of interest to physicians and nurses commencing training in anesthesiology Certain parts of the book may be of interest to medical students

The book is divided into three parts The first part considers the pharmacology and clinical application of individual drugs in current use The pharmacologic data is largely clinical and embodies observations on surgical patients In instances in which data concerned with the effects of anesthetic drugs on man are not available laboratory data are cited The second part deals with various diseases complicating the surgical condition, their relationship to anesthesia and the manner in which physiologic disturbances caused by anesthetics affect these diseases The third part deals with the choice of anesthesia in relationship to the operation to be performed The interrelationships between anesthesia and the surgical disease, the physical status of the patient and the technical requirements of surgery are considered

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# Selection of Anesthesia

# INTRODUCTION

Although the number of physicians specializing in anesthesiology in the United States is increasing rapidly, the majority of anesthetics are still administered by persons other than physicians With few exceptions, the non medical anesthetists are graduate nurses who have been instructed in the technical aspects of the administration of inhalation and intravenous anesthesia Under this system the surgeon is responsible for the selection and conduct of anesthesia In theory he selects the drug and directs its administration Actually, in most instances, the nurse does it all, because she appears to be better versed than the surgeon in the technical as well as the pharmacologic aspects of the subject As a result, the nurse is allowed to proceed in whatever manner she chooses or sees fit Adoption of routines in the selection of anesthesia is thus encouraged by this situation The same anesthetic technique is employed for all procedures of a given kind with little regard to individual variations, indications and contraindications When the patient's physical state is excellent, the choice of one drug or method over another may not influence seriously the course of events for the more simple standardized surgical procedures such as hernіaplasties, appendectomies, and hysterectomies The surgeon is satisfied as long as anesthesia appears satisfactory As long as the airway remains unobstructed and overdosage is avoided, the general course of events apparently is uneventful, and the outcome of the operation is successful However, the situation in surgery is now changing Modern surgery is no longer limited to simple, standardized procedures In recent years surgeons and anesthetists have been faced with problems of increasing complexity Methods of diagnosis, of pre operative and postoperative management of patients, and of techniques in anesthesia and surgery have undergone striking improvements Greater skill on the part of all members of the surgical team is necessary In the past, surgery was primarily anatomic and emphasis was placed on structure Today physiology is stressed and the emphasis has shifted to function As a consequence, the present day surgeon must be well versed in both physiology and anatomy The importance of fluid balance, hemodynamics, hormonal effects, and the role of the autonomic nervous system on the outcome of surgical operations, are being given greater cognizance Surgeons are no longer timid in performing intrathoracic or mediastinal explorations, pulmonary resections, operations upon the heart and great vessels, and combined abdomino thoracic procedures Likewise, advances in therapeutics have improved the prognosis of surgical patients who have medical complications such as cardiac disease, hypertension, diabetes, and so on Certain so called poor risk patients, who were termed

# PART I

## PHARMACOLOGICAL BASIS FOR THE SELECTION OF ANESTHESIA

inoperable and denied the benefits of surgery, are now operable Attention is also directed towards the manner in which disease alters both body structure and function, and towards the effects of surgery and anesthesia upon these pathologic changes

Last but not least, consideration of the effects of anesthesia upon normal body function is emphasized It is well recognized that an anesthetic does more than merely cause unconsciousness and provide muscle relaxation The *pharmacologist, the physiologist, and the experimental surgeon have demonstrated* clearly that anesthetic drugs cause far reaching physiologic disturbances, even without surgery Furthermore, technical difficulties of anesthesia superimpose additional effects

Thus, the individual upon whose shoulders the responsibility rests for the selection of anesthesia can no longer afford to ignore the fundamental principles of the science of anesthesiology

# PART I

# PHARMACOLOGICAL BASIS FOR THE SELECTION OF ANESTHESIA

# I

# BASIC CONSIDERATIONS IN SELECTING ANESTHESIA

## FACTORS IN SELECTION OF ANESTHESIA

There is no such thing as the formulation of a routine in the selection of anesthesia Most individuals seek information concerning the selection of anesthesia, with the prospects of obtaining a simple, general formula which is applicable to all situations arising in clinical practice However, as is the case with other problems encountered in medicine, selection of anesthesia cannot be empiric, but requires individualization Various factors are involved, some of which are variable, and are altered from one situation to the next In general, five factors must be considered in selection of anesthesia (1) The nature of the operation (2) The skill of the surgeon (3) The skill of the anesthetist (4) The status of the patient (5) The pharmacologic effects of the drugs used

### Nature of the Operation

First, and the most obvious, is the nature and extent of the contemplated operation Certain questions must be answered concerning the procedure Will it be prolonged or will it be brief? Will it be accompanied by unavoidable trauma or blood loss? Will there be stimulation which initiates various reflexes? Will it merely necessitate pain relief or is muscle relaxation an additional requirement? If the former is the case, it is possible for example, that ethylene or nitrous oxide with a basal narcotic, or cyclopropane alone, may suffice If the latter, ether, spinal anesthesia or a combination of drugs capable of yielding muscle relaxation besides the pain relief must be used The site of operation is of considerable importance from the standpoint of anesthesia Operations about the head and neck or upper extremities usually necessitate the use of and are best performed with general anesthesia Surgical procedures on the lower extremities may be performed with spinal or other forms of regional block Certain operations require the prone, lateral or other awkward positions In these, intratracheal anesthesia is necessary to insure adequate control of the airway In intrapleural and mediastinal operations and in other instances in which positive pressure is required, intratracheal anesthesia is mandatory The use of intratracheal anesthesia limits the number of drugs from which to choose, because not all are satisfactory for intubation

## Status of the Patient

The second factor to be considered is the status of the patient The *presence or absence of pathologic states other than the disease for which* the operation is being performed, together with the possible bearing of these disease states upon the progress and outcome of the operation, are important considerations The presence of diabetes, for instance, makes the clinician mindful of acidosis Drugs and techniques of administration must be selected which least disturb metabolism, fluid, and electrolyte balance, and which fulfill the requirements of anesthesia necessary for the operation The question is often not so much what is best, but what will harm the patient least

## Skill of the Surgeon

The third factor, one of extreme variability, is the skill of the surgeon *The difference between surgeons who work quickly and unhesitatingly* and those who are slow, hesitant, and indecisive can only be fully appreciated by surgical assistants and other operating room personnel Some operators perform surgery deftly under conditions of moderate relaxation provided by the average depth of ether anesthesia Others are handicapped unless the patient is in a cadaver like state Inasmuch as the anesthetic is merely an adjunct to the operation, it is selected primarily from the standpoint of permitting the operator to utilize his utmost skill without handicap Too frequently consultants are unfamiliar with the surgeon's capabilities They are thus at a disadvantage *in attempting to suggest choices of drugs and* techniques of administration The anesthesiologist has an advantage over his colleagues in this respect because he devotes his attention exclusively to anesthesiology and is in constant association with the surgeon He is familiar with the surgeon's habits and whims as well as his technical skill He is in a position to select and administer an anesthetic which provides operating conditions best suited for a particular surgeon

## Skill of the Anesthetist

The fourth factor to be considered is the skill of the anesthetist As in the case of knowing the surgeon, again the consultant is at a disadvantage because he rarely is familiar with the anesthetist and in many cases does not even know who he will be The skill of the anesthetist, particularly in formidable operations and *in poor risk patients, is of such importance that it is* often the difference between success and failure Fatalities in the operating room are almost always laid at the doorstep of either the surgeon or the anesthetist The results of a surgeon s error usually appear in the post operative period Peritonitis from an accidental perforation of the bowel, slough or gangrene from impairment of the blood supply to an organ and other sequelae *of technical errors do not manifest themselves immediately* Uncontrollable hemorrhage and irreversible shock are errors which may be responsible for an unexpected fatality on the operating table The anesthe

tist's errors are almost always immediately apparent Overdosage of an anesthetic drug, spinal shock, asphyxia from obstruction, aspiration of vomitus, pus or blood, and other technical errors are so often responsible for "sudden death" The effects of technical mismanagement of anesthesia may become superimposed upon the effects of surgery and contribute to a stormy postoperative course with a possible fatal outcome Atelectasis, shock, and other postoperative complications may be due in part or entirely to the effects of anesthesia Here again the consultant is at a disadvantage, unless he is aware of the anesthetist's capabilities and is familiar with the technical problems and difficulties involved in a contemplated anesthetic The patient who has heart disease, for example, fares better, theoretically, from the standpoint of the myocardium when ether is selected, rather than spinal anesthesia or cyclopropane Although ether is depressant to the myocardium and conducting tissues, it disturbs the cardiovascular system less than other major anesthetics Still, the induction of ether anesthesia is not simple and it requires considerable skill to make it atraumatic When attempted by a novice, the induction consumes considerable time Undue trauma may be inflicted by coughing, straining and anoxia from the partial obstruction which invariably occurs Certainly these may be detrimental even to patients with minimal cardiac lesions An uneventful induction with a non irritating, rapid acting drug such as cyclopropane, followed by ether, would impose less hardship upon the patient, even though it is recognized that cyclopropane affects cardiac automaticity and should on theoretical grounds be excluded

## Pharmacologic Action of the Drugs

The last but not least important factor is the pharmacologic action of the selected drug and its effect upon the patient One must consider the effects both during the operation and in the postoperative period

Obviously then, the problem of selecting the anesthetic for a contemplated procedure cannot be dismissed by simply invoking a rule If the consultant assumes that both the surgeon and the anesthetist possess maximum skill and judgment, the problem of making a choice is purely on a pharmacologic basis

The drugs used by anesthesiologists fall into three categories (1) Nervous system depressants—these comprise the majority of drugs used (2) Nervous system stimulants—these are used to antagonize the depressants (3) Adjuncts to anesthesia—these are used to counteract undesirable side effects caused by anesthetics Procaine amide, for example, counteracts an enhancement of cardiac irritability Atropine inhibits secretions of mucous and vagal activity Ephedrine overcomes hypotension, and so on Each of these three groups of drugs are described subsequently

### REFFRENCES

ADRIANI J Pharmacological basis for the election of anesthesia *New Orleans M &S J* 95 266-273 1942

GUEDEL A F *Inhalation Anesthesia* New York Macmillan 1950

TABLE I

General properties and characteristics of currently employed anesthetic drugs

| Name | Chemical Name | Formula | Description | B.P. or M.P. | S.G. | Stability | Preservative | Packaged | Accepted | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|
| Ether | Diethyl oxide | $C_2H_5$–O–$C_2H_5$ | Colorless mobile inflammable liquid with pungent odor | B.P. 36 37 C | Liq 718 at 15 C; Vap 2 6 | Oxidized by air or oxygen, light or heat to peroxides | Copper or iron | Dark bottles, cans | U.S.P. | Contains up to 4% alcohol from manufacturing process |
| Vinethene | Vinyl oxide | $C_2H_3$–O–$C_2H_3$ | Colorless inflammable liquid with garlic-like odor | B.P. 28–29 C | Liq 77 at 20° C; Vap 2 2 | Polymerizes to resins. Decomposed by acids | Basic substances, amines or other | Dark bottles | U.S.P. | Contains 4% added alcohol to elevate boiling point |
| *Chloroform* | *Trichlor* methane | $CHCl_3$ | Sweet *pungent* liquid yielding heavy vapor | B.P. 60–61 C | Vap 4 12 | Oxidized by air, oxygen, light or heat. | Ethyl alcohol. | Dark bottles. | U.S.P. | Contains added alcohol to act as a preservative |
| Ethyl chloride | Monochlorethane | $C_2H_5Cl$ | Colorless mobile highly volatile liquid | B.P. 12 5 15 C | Liq 921 at 0° C; Vap 2 28 | Hydrolized to alcohol and hydrochloric acid | None added | Dark glass or metal amplon | U.S.P. | Contains alcohol from manufacturing process. |
| Trilene | Trichlorethylene | $C_2HCl_3$ | Sweet pungent mobile liquid | B.P. −8 C | | Oxidized by oxygen, light, heat and soda lime | Thymol | Dark bottles | U.S.P. | |
| Paraldehyde | Polymer of acetaldehyde | $(CH_3CHO)_3$ | Colorless mobile liquid with pungent clinging odor | B.P. 121 122° C | Liq 999 at 0 C | Converted to acetaldehyde. Very slowly decomposed by acids. | None added. | Dark bottles. | U.S.P. | May contain traces of acetaldehyde |
| Amylene hydrate | Tertiary amyl alcohol | $C_5H_{11}$–OH | Colorless mobile liquid | B.P. 98–100° C. | | Stable. | None added | Dark bottles | U.S.P. | Used as solvent for tribromethanol to form amylene hydrate |
| Trichlorethanol | 1 Hydroxy 2 Trichlorethane | $CCl_3CH_2OH$ | Colorless liquid. | B.P. 151 C at 751 mm Hg | Liq 1 555 at 20 C | Oxidized to aldehydes and hydrobromic acid. Decomposed by heat, light, air | Keep cool away from light | Dark bottles | | Sparingly soluble in water but will make a 3% solution at 37 C |
| Tribromethanol | 1 Hydroxy 2 Tribromethane | $CBr_3CH_2OH$ | White powder which sublimes with decomposition | M.P. 80° C | | Oxidizes to aldehydes and acids decomposed by heat, light, air | Keep cool away from light, heat, air | Dark bottles. | U.S.P. | 1 gram dissolves in ½ cc of amylene hydrate to form 1 cc of avertin fluid |
| Ethylene | Ethene | $C_2H_4$ | Colorless gas with an ethereal odor | B.P. 103° C. | Vap 97 | Stable at ordinary conditions. | None added, keep in a cool place | Compressed into a liquid and stored in steel cylinders. | U.S.P. | Carbon monoxide a possible impurity |
| Cyclopropane | Trimethylene | $C_3H_6$ | Colorless, sweet smelling gas. | B.P. −34 C | Vap 1 46 | Stable at ordinary temperatures and pressures | None added, keep in cool place | Compressed into a liquid and stored in light metal cylinders | U.S.P. | A polymer of propylene in presence of iron at 100° C may be converted to propylene |
| Nitrous oxide | Nitrogen monoxide | $N_2O$ | Colorless, sweet smelling gas | B.P. −89 C | Vap. 1 54 | Stable | None added, keep in cool place | Compressed into a liquid and stored in heavy metal cylinders | U.S.P. | Nonflammable but supports combustion |

## CHEMICAL NATURE OF DEPRESSANT DRUGS

Even though clinicians seldom refer to drugs according to their chemical groupings, some understanding of their chemical nature is essential for intelligent and proper utilization With the exception of the magnesium salts, the bromides, and nitrous oxide central nervous system depressants are organic compounds containing carbon, hydrogen, oxygen, nitrogen and, in some cases, sulphur

Volatile drugs are, with few exceptions, aliphatic, straight chained hydro carbons or ethers Non volatile, drugs are aliphatic, heterocyclic or aromatic derivatives The aliphatic derivatives are usually alcohols, aldehydes or ketones The distinction between volatile drugs and non volatile drugs is em phasized, because a pharmacologic difference exists between the two types ✓The volatile drugs possess marked powers of analgesia and cause anesthesia The non volatile drugs are sedatives, hypnotics, basal narcotics, and nar cotics They possess little or no analgesic power and, are as a rule, not satis factory when used alone for obtaining anesthesia

The majority of currently employed local anesthetics are complex, hetero cyclic, and aromatic nitrogen containing bases Certain substances used in conjunction with anesthesia are obtained from plants The majority of these are vegetable bases or alkaloids The chemical nature of the currently used drugs will be elucidated in more detail under the discussions of each indi vidual drug or groups of drugs (Table I)

## CONTROLLABLE AND NON CONTROLLABLE ANESTHETICS

Inhalation anesthetics are often termed "controllable anesthetics," be cause depth may be varied at will by altering the inspired concentration This in turn alters the alveolar and blood concentration upon which the cellular concentration depends The blood concentration of a volatile drug is a reflection of the cellular content of the drug and an index of the depth of anesthesia The non volatile central nervous system depressants by con trast are *"non controllable,"* because they are administered in a single pre judged dose orally, rectally, intramuscularly or intravenously The blood concentration is not easily varied once the drug has been administered and absorbed One must depend entirely upon mechanisms for detoxification and elimination for altering cellular content The blood level is not neces sarily an index of the depth of narcosis or the concentration in the body Certain non volatile drugs are promptly removed from the blood stream and stored in the fat, muscle and other tissues and are gradually released and eliminated or detoxified The blood level is variable It may be high im mediately after administration when the state of depression is mild and it may be barely detectable later even though marked depression exists

## REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 19›› pp 3–7

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 27

SAKLAD M Grading patients for surgical procedures *Anesthesiology* *2* 281 1943

SEEVERS M H and WATERS R M Pharmacology of anesthetic gases *Physiol Rev* *18* 447 1938

III

# VOLATILE ANESTHETICS

In order to be effective and useful for inhalation anesthesia a drug must be a gas or a liquid which volatilizes easily. Liquids possessing anesthetic properties, which boil at a point over 60 C, are not suitable, as a rule, for inhalation because the vapor pressure at room temperature is usually insufficient to maintain the necessary depth of anesthesia. Chloroform which boils at 61 C vaporizes with difficulty at room temperatures. It is effective because the concentration necessary for surgical anesthesia is low. Chloroform is the most potent of the inhalation anesthetics. Its potency offsets the disadvantage of poor volatility. Ethyl ether boils between 36 and 38 C depending upon the alcohol content. Vinyl ether boils at 28 C and ethyl chloride at 12 C. All three volatilize easily and are suitable for inhalation anesthesia.

## Essential Requirements of an Anesthetic

The chief requisites of any anesthetic are (1) That it affords complete pain relief, (2) that it abolishes superficial reflexes, and decreases or abolishes muscle tone, and (3) that it causes hypnosis or unconsciousness. The first two are absolute requirements. Amnesia or hypnosis is an additional desirable feature from a psychic standpoint but it is not absolutely essential to painless surgery and satisfactory operating conditions.

All anesthetics exert some deleterious effects upon the organism and interfere with or inhibit many physiologic functions. As the amount administered is increased ultimately a concentration is reached which causes death. In other words anesthetics are protoplasmic poisons. The term *ideal anesthetic* frequently used by clinicians, refers to certain desirable features which a volatile drug should possess. (1) It should be pleasant and easily inhaled. (2) It should be chemically stable and should not decompose within the body. (3) It should be easily eliminated, preferably unchanged. (4) Its action should be reversible. After it has been eliminated the cellular functions should revert to their former status without impairment. (5) It should possess sufficient narcotic potency to yield all depths of anesthesia. (6) It should allow adequate oxygenation. None of the currently available anesthetics possesses all these requisites. The ideal anesthetic remains to be discovered.

## Mode of Action of Depressant Drugs

Central nervous system depressants act as follows. (1) They have a special predilection for nervous tissue, (2) they depress all types of cells

in sufficient concentration, and (3) there is a reversal to normal activity when the drug is withdrawn Possibly the affinity for nerve tissue is explained by the lipophilic nature of these drugs Nervous tissue has a high lipoid con tent compared to other tissues In addition, the nervous system has a rich blood supply Both factors favor saturation of the brain prior to saturation of other tissues Consequently concentrations, which depress the nervous system, are not necessarily present in non nervous tissues in sufficient amounts to inhibit the functions of organs so composed The exact mech anism by which anesthetic drugs cause depression of cellular activity is not known Indeed, one is not certain that any one single mechanism causes the change in function For a discussion of the theories of narcosis, one is referred elsewhere to the numerous reviews and discussions on the subject

REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 19
ADRIANI J *The Chemistry of Anesthesia* Springfield Thomas 1946 Ch VI XII
BURSTEIN C L *Fundamental Considerations in Anesthesia* New York Macmillan 1950
GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 pp 29–33
GUEDEL A E *Inhalation Anesthesia* New York Macmillan 1950
SEEVERS M H The narcotic properties of carbon dioxide *New York State J Med, 44 597 1924*

## ABSORPTION AND ELIMINATION OF VOLATILE DRUGS

### Fate of Volatile Drugs in the Body

With few exceptions, most volatile drugs used for inhalation anesthesia are inert and undergo no changes in the body Elimination is entirely through the lungs, except for a relatively small portion which passes into the urine, feces, vomitus, saliva and perspiration The absorption, distribution and elimination are the same as, and follow the physical laws pertaining to the behavior of, non anesthetic inert gases in the body The vapors of a volatile drug behave in the same manner as a gas in these respects Gases and vapors exert a pressure or tension in an inhaled mixture in the alveoli, the blood, and in the interstitial and intracellular fluid All drugs must possess some degree of water solubility in order to reach and pass into the cells

### Pressure Gradient

During induction a pressure gradient is established from the inspired mixture to the alveoli then to the blood and next to the cells (Fig 1) Dur ing maintenance theoretically an equilibrium is established between the cells, blood alveolar air, and inhaled mixture Actually, an equilibrium i never attained due either to losses through excretory channels or to inad equate absorption At the conclusion of anesthesia, when the subject breathes room air, the tension of the anesthetic gas or vapor in the inspired air i

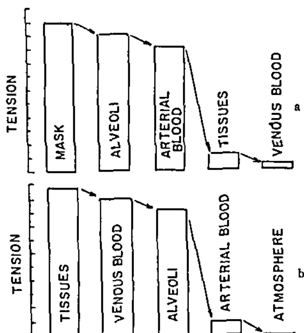



FIG 1 (a) The pressure gradient during induction of anesthesia with a volatile anesthetic The gas passes from the pharynx to the alveoli where the pressure is less to the arterial blood where the tension is still less and into the tissues where it is zero at the onset Theoretically during maintenance an equilibrium is established between the arterial blood the tissues and the venous blood When anesthesia is discontinued the pressure gradient is reversed (b) It becomes zero at the lips upon removal of the mask The gas then passes from the tissues to the venous blood to the alveoli to the lips Then tensions in the arterial blood and in the alveoli at the end of inspiration are nearly the same

zero Then the pressure gradient is reversed, from the tissues, where the tension is the highest, to the blood, to the alveoli, and to the lips where it is zero The drug is then eliminated

## Factors in Absorption and Elimination

The factors which influence the absorption and elimination of volatile anesthetics are (1) The tension or concentration in the inspired mixture, (2) the tidal exchange, (3) the minute volume exchange, (4) the functional residual air volume, (5) the solubility coefficient of the drug in blood and tissue fluids, (6) the diffusibility through the alveoli, (7) the blood flow through the lungs, (8) the blood flow through the tissues, and (9) the solubility in the tissues Obviously the higher the gas tension which exists in the blood, the greater will be the pressure gradient which is established, and the more rapid will be the saturation An adequate tidal exchange is necessary to allow proper mixing of the drug with the functional residual air The functional residual air volume is an important factor because this represents the total gas volume which comes into contact with the alveoli When the functional residual air volume is low and approaches the tidal volume, more abrupt changes occur in the alveolar concentration with each respiration This situation is encountered in children Any momentary increase or decrease in concentration is immediately reflected in the blood level and anesthesia lightens or deepens When the functional residual air volume is increased in relation to the tidal exchange, adequate and rapid mixing is impaired The desired alveolar tension is attained slowly Elimination of the drug is slower also Increasing the minute volume exchange increases the total amount of drug carried to the lungs and facilitates blood and tissue saturation

## Effects on the Alveoli

Volatile anesthetics pass with ease through the alveolar membrane in the same way *as do oxygen, nitrogen, helium or other gases. The membrane is* not altered in any way whatever. A drug which perchance would exert a deleterious effect would not be clinically useful. Reference is occasionally made to a volatile anesthetic being "irritating," the inference being that the alveolar *membrane is in some way altered or damaged. Vapors of ether and* other volatile drugs stimulate the vagal nerve endings in the alveoli causing exaggerated breathing. The mucous and salivary glands in the mouth, pharynx, and trachea are stimulated to increased secretory activity. These responses are interpreted mistakenly as "irritation."

## Solubility in Tissues

*The coefficient of solubility of the drug in blood is important.* The more soluble the anesthetic is in the blood, particularly when it is of low potency, the more the quantity which will be necessary to saturate the blood to maintain anesthesia. To be useful a drug must possess sufficient solubility in *water to be carried in adequate amounts for anesthesia to the cells.*

Blood flow through the tissues and circulation time through the lungs play a role in absorption and elimination, but are unimportant relatively speaking. Even though the peripheral blood flow is slowed, as in cardiac failure, blood passes through the lungs *with sufficient* speed to absorb volatile drugs. The blood flow through the brain and other tissues is a more important factor however. The saturation and desaturation of adipose tissue occurs slowly, despite the fact that anesthetic drugs are lipophilic, because *these* tissues possess a poor blood supply. Minute amounts of cyclopropane may be detected in the blood for many hours after the termination of anesthesia. This comes from the lipoid tissues which are releasing the anesthetic, which *has been absorbed. The release is slow due to the poor blood supply.* All the cyclopropane is eliminated from the blood and watery tissues within ten minutes because of its low water solubility. The brain, when compared to adipose tissue, possesses an excellent blood supply, although the lipoid content is less, relatively speaking. Brain tissue becomes saturated and desaturated more rapidly than adipose tissue. Brain absorbs more drug than muscle, for example, because of the differences in lipoid content of the two tissues. *On the other hand ether is relatively more soluble in* water than cyclopropane. As a result both the lipoid tissues and the watery tissues absorb considerable amounts.

## Equilibrium Between Blood, the Cells and Alveolar Air

An equilibrium is ultimately established between the cells of the body, the blood, and the alveolar air, if the anesthetic is *administered* over a long period of time. The brain comes to equilibrium with the blood first and con

sciousness is lost Ultimately the other tissues come to equilibrium In the meantime, as the anesthetic is being absorbed by the tissues, more must be added to the inhaled mixture to make up for that being withdrawn from the blood Unless this is done, equilibrium between the brain and the blood is disturbed, the concentration in the brain cells is reduced and anesthesia lightens The equilibrium ratio between the alveolar air and the blood (air-blood ratio) varies with each drug, the body temperature, partial pressure, and other factors For ether the ratio is 1 in blood to 15 in air That is, when equilibrium is established between alveolar air and blood, alveolar air contains one unit of ether, blood 15 In the case of cyclopropane the figure is reversed 1 to 0 4 That is, when equilibrium is established alveolar air contains 1 unit, blood 0 4 During recovery the partition is on this basis In other words the venous blood returning to the lungs imparts to the alveolar air one unit of its ether and retains 15 On the other hand cyclopropane imparts one unit and retains 0 4 unit It can be seen that the elimination of cyclopropane will be more rapid than that of ether

REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 pp 3-7

ADRIANI J *The Chemistry of Anesthesia* Springfield Thomas 1946 Ch XXX

SEEVERS M H *et al* Comparative study of cyclopropane and ethylene with reference to body saturation *J Pharmacol & Exper Therap* 53 295 1935

SEEVERS M H and WATERS R M Pharmacology of anesthetic gases *Physiol Rev* 18 447 1938

## METHODS OF ADMINISTRATION OF VOLATILE DRUGS

### Devices Used for Administration of Volatile Drugs

Special devices known as inhalers are necessary for the administration of drugs by inhalation All inhalers have three features of importance (1) A source of oxygen (2) a means of eliminating carbon dioxide, and (3) some means of supplying the proper concentration of drugs at the lips and nostrils The methods of administration are classed as *open* or *closed* In the open methods, the gases or vapors are conducted into the naso and oro pharynx or to the nostrils and lips by catheters In the closed methods the gases and vapors are confined in a device which permits their inhalation through a mask In the open methods the gases and vapors mix with and escape into the atmospheric air In the closed method there is no mixing with atmospheric air Anesthetists refer to the methods of administrating volatile drugs as (1) *open cone*, (2) *semi open* with a cone (3) *insufflation*, (4) *semi closed* and (5) *closed* with total rebreathing

### Open Methods

The open cone technique is applicable to volatile liquids (Fig 2) The liquid is vaporized on gauze supported by a metal framework It is mixed

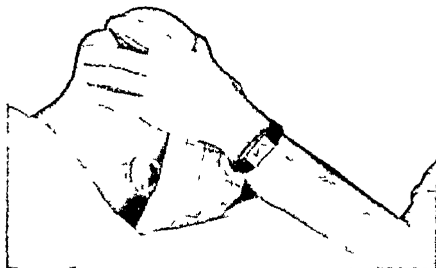


FIG 2 The "Open Cone" technique of administering volatile anesthetic drugs

with air which serves as vehicle, a diluent, and a source of oxygen Carbon dioxide escapes through the mesh of the gauze The semi open method differs little from the open An enclosure, usually a towel wrapped around the mask, prevents escape of the vapors and provides some rebreathing (Fig 3) Insufflation is suitable for both gases and vapors The gases are conducted, mixed with oxygen, into the nasopharynx and oropharynx by means of catheters or other tubes Liquids are vaporized and the vapor is mixed with

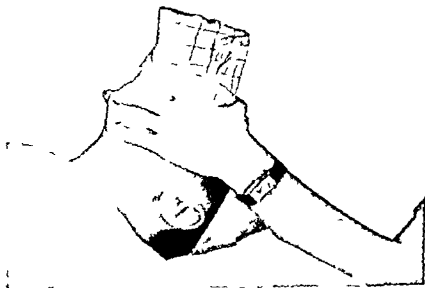


FIG 3 Semi-Open Technique of Anesthesia by the Open Drop Method for Volatile Liquid Note that a towel is arranged in a chimney like fashion about a wire frame over which is draped gauze upon which the drug is dropped The towel provides a partial enclosure for the vapors of the drug Some reduction in oxygen tension and retention of carbon dioxide occurs

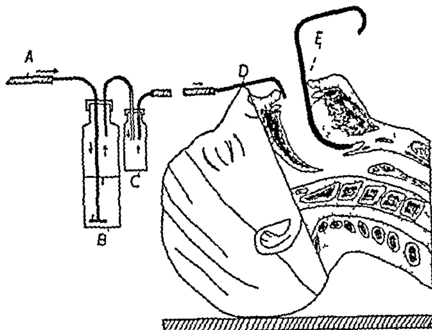



Fig 4 The diagram illustrates the oral insufflation of vapors of volatile liquids (A) The source of compressed gas u ually air or oxygen (B) Container for the volatile drug (C) Trap interposed between apparatus and pharynx to prevent liquid from accidentally passing over into the respiratory passa es (D) Cannula for delivering the vapor into the pharynx (F) A blade or tongue depressor to support the tongue and provide an airway when surgery is being performed in the mouth This technique is u ed for oral and nasal surgery

air oxygen or other gases and conducted to the upper respiratory passages in the same manner (Fig 4)

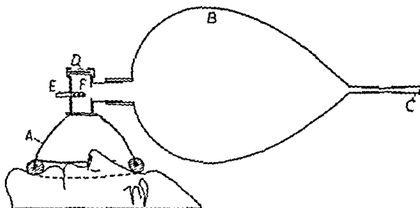
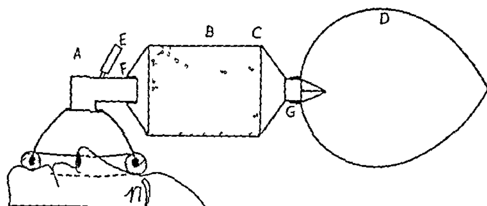


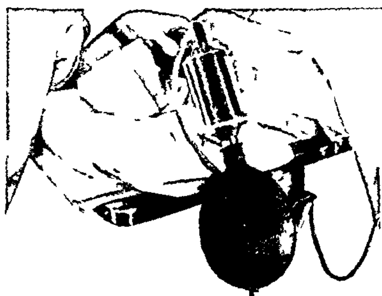

Fig 5 The s mi closed inhaler is composed of a closed mask (A) and a breathing bag (B) The bag acts as a reservoir for inspired gases A continuous flow of gases is admitted into the apparatus from the source of supply into the inlet tube (C) The exhalations excess gases and vapors escape throu h the adjustable valve (D) A variable amount of re breathing occurs in this type unless an additional valve is placed at the inlet from the breathing bag into the mask (A) Most inhalers are equipped with an obturator (E) or valve which allows the mask to be clos d from the ba and be filled with gas until apparatus i ready for use The patient may breathe room air through the vents (F) provided for the purpose which are opened when the obturator is closed off from the mask

## Semi Closed Method

The semi closed device consists of a mask and a reservoir, usually a 5 liter rubber bag containing the desired mixture With each inspiration the patient draws an amount of mixture equal to his tidal volume from the reservoir The exhaled gases are ejected to the outside air through a valve on the mask (Fig 5) Semi closed devices may be arranged as *non rebreathing types* by interposing a valve between the mask and the reservoir The valve permits a unidirectional flow from the bag into the mask but not in the reverse direction Omission of the valve permits *rebreathing* Unless a flow of gas equiva




a



b

Fig 6 (a) The to and fro inhaler is composed of a mask (A) a canister (B) which is charged with soda lime (C) and a breathing bag (D) During expiration the gases pass over the soda lime to the breathing bag During inspiration the direction is reversed The respired gases are thus passed over the absorbent twice The slip joints (F) and (G) allow the inhaler to be dismantled and the canister to be removed so that rebreathing of carbon dioxide is possible if desired The inlet (E) admits vapors and gases from the vaporizers

(b) The to and fro inhaler shown in use on a patient The to and fro inhaler is *more difficult to* use technically than the circle filter

lent to the tidal volume of the subject is supplied in the rebreathing type, carbon dioxide accumulates in the apparatus and the oxygen is depleted so that suboxygenation occurs. Some semi closed devices operate on the "demand principle." The negative pressure caused by inspiration in the mask activates a valve which (from a reservoir in which the gas is stored under pressure) releases an amount of gas equivalent to the patient's tidal exchange. Semiclosed devices are used for the administration of oxygen carbon dioxide mixtures and for the "washing out" of nitrogen from the tissues. During the induction of nitrous oxide or ethylene anesthesia, the semi closed method is mandatory to permit "washing out" and replacement of the nitrogen in the alveoli by the gas. Both gases require a partial pressure of over 575 mm Hg in the alveoli to be effective. Unless nitrogen is eliminated the tension necessary for anesthesia cannot be administered. The open and semi open methods are wasteful, are not entirely physiologic, and create fire hazards.



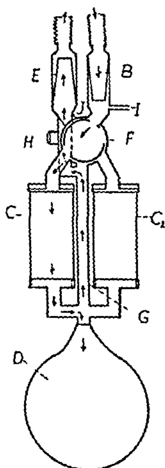
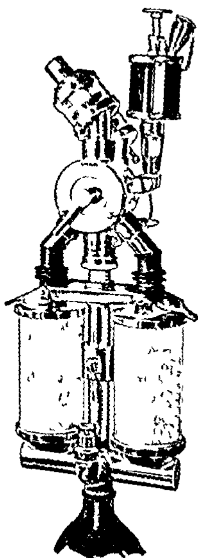




Fig 7 The circle filter. During expiration the gas passes from the mask (A) into a corrugated tubing approximately 3 feet long then through a valve (B) over the absorbent in the canister (C). When inspiration takes place the gases are drawn from the bag (D) through valve (I) through the second or inspiratory corrugated tubing back to the mask. Thus a circuit is completed.

Two canisters are provided in order that one may be refilled during the operation or that one be available if one becomes exhausted. This type apparatus is used by approximately 95 % of the anesthetists in the United States.



when flammable mixtures are used Devices known as *flowmeters* are necessary to measure and mix gases in proper proportion Flowmeters are not necessary for volatile liquids administered by the open methods

## Closed Methods With Rebreathing

The closed methods permit enclosure of gases by means of a tight fitting face piece or a connection from the inhaler to tracheal catheters Carbon dioxide is absorbed by chemicals, usually soda lime, oxygen is supplied to meet the metabolic requirements of the subject, usually at a rate of 300 cc per minute This type of closed inhaler does not communicate with the outside air Two types of closed inhalers are used—the *"to and fro"* type (Fig 6) and the *"circle"* type (Fig 7) The latter is used by approximately 90 per cent of the anesthetists in the United States Each type has its advantages and disadvantages The closed system permits inhalation of warm gases, enclosure of flammable gases use of positive pressure, maintenance of a constant level of anesthesia, satisfactory control of both oxygen and carbon dioxide tensions in the inspired gases, and economy of volatile drugs More skill is required in the management of the closed systems than the open A misconception which seems to be accepted as an established fact is that the open drop method, notably open drop ether, is the best type of anesthesia, particularly in poor risk patients The closed methods, when used by experienced individuals are far superior to the open The open drop method may be safer when used by the novice but is certainly far from the best and is the least desirable

### REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 20

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 pp 22–100

CULLEN S *Anesthesia in General Practice* Chicago Yr Bk Pub 1946

FAULCONER A and LATTERAL K E Tensions of oxygen and ether vapor during the use of semi-open air ether method of anesthesia *Anesthesiology* 10 247–258 1949

LUNDY J S *Clinical Anesthesia* Philadelphia Saunders 1942

GUEDEL A E *Inhalation Anesthesia* New York Macmillan 1950

# STAGES OF ANESTHESIA

## Effects of Volatile Drugs on the Nervous System

When anesthesia is induced with currently available inhalation anesthetics, four stages are recognized in the transition from consciousness to complete abolition of reflex activity The impression that these four stages are well demarcated and delineated is incorrect One stage gradually merges into the next In establishing surgical anesthesia, the anesthetist is guided by changes in three systems, the *central nervous system*, the *respiratory system* and the *circulatory system* Other physiologic units are involved also

but the attention of the anesthetist is focused upon these three systems. The disappearance and reappearance of certain superficial and deep reflexes are guides to variations in depth of anesthesia. Some of the most reliable signs of depth of anesthesia may be noted in the eye. Fortunately the anesthetist is at the patient's head and is in a position to observe these reflexes. The disappearance of the lid reflex, the variations in activity of ocular movements and the activity of the pupillary and corneal reflexes are constantly observed during inhalation anesthesia. The character of respiration is a valuable guide to the degree of central nervous system depression. Small muscles lose their activity before large muscles. The intercostals are small by comparison to other muscles. Loss of intercostal activity places the burden of pulmonary ventilation upon the diaphragm. The piston-like action of the diaphragm causes an abrupt change in intrathoracic pressure. A quickened inspiration and a prolonged gradual expiration are manifestations of this loss of intercostal activity. The gradual expansion of the thoracic cage causes changes in intrathoracic pressure to be less abrupt. Inspiration and expiration are nearly equal in amplitude and duration when the intercostal muscles are active. Respiration simulates that observed in normal sleep. Loss of intercostal activity indicates a decrease in tone of the larger muscles, particularly by the recti and those of the extremities. Circulatory changes caused by anesthesia per se are not apparent until the level of anesthesia is profound. The pulse rate, systolic and diastolic pressures are observed at frequent intervals by the anesthetist throughout the operation.

## Stage I—Analgesia

The first stage (designated by Roman numerals) is termed the *stage of analgesia*. The subject is unable to perceive pain, cold, warmth, and light touch. Special senses may be partly obtunded and a sensation of numbness is described. Superficial and deep reflexes remain active. The sensorium remains clear. Consciousness is impaired only to a slight degree, if at all. These changes may be demonstrated by allowing the subject to inhale equal parts of oxygen and nitrous oxide for several minutes and then stimulating the skin with a sharp instrument. There is a quick withdrawal from the stimulus. However the stimulus is not interpreted as painful. It does evoke a reflex and the subject is aware of being stimulated. Pain relief of this sort without abolition of reflexes is inadequate for any but the most minor surgery.

## Stage II—Delirium

As the concentration of nitrous oxide is increased further depression of the central nervous system occurs and the subject then merges into the second stage. This stage is often termed improperly the *excitement stage* or the *stage of delirium*. No abrupt transition or well delineated separation occurs

between stage I and stage II The sensorium is clouded and consciousness is gradually lost Muscle tone is increased, probably due to release of cortical inhibitions, which allows the subcortical centers to have full sway The superficial reflexes are exaggerated Inhibitions are lost and extraneous stimuli may initiate violent movements, struggling and straining Injury may occur in this stage, so restraints and other precautions to safeguard the patient are necessary Restraining straps for the arms and legs are mandatory and *not objectionable to properly sedated patients An attendant should be* on hand to assist the anesthetist in the event such struggling occurs The second stage may be rapidly transcended and rendered uneventful by pre anesthetic administration of sedatives, hypnotics or narcotics The second stage is unduly prolonged in unsedated, apprehensive, highly emotional subjects and in chronic alcohol addicts A second stage, which could be uneventful and of brief duration, is frequently converted to one which is prolonged and stormy because the subject is stimulated and improperly managed before stage III is attained

The importance of adequate and properly timed pre anesthetic sedation and the avoidance of all stimuli whether visual auditory or tactile during the induction period cannot be stressed too strongly Adjustment of belts straps, introduction of cannulae, catheters, physical examinations, in short, anything which *requires stimulating the patient initiates excitement* A prolonged second stage is often characterized by incoherent mumbling, crying or talking swallowing, and the secretion of thick mucus Due to the excitement sympathetic stimulation occurs, the pupil are widely dilated the blood pressure rises, a tachycardia ensues Respiration is stertorous, jerky and irregular due to release of cortical inhibitions Breathholding or brief periods of apnea are not uncommon The latter is due to hypocapnia from hyperventilation, which is not uncommon Such periods of apnea are often mistaken for overdosage and alarm the uninitiated anesthetist The olfactory and visual senses are inactivated early in the second stage The auditory senses are abolished after the visual early in the second stage It is not uncommon for patients to recount comments of by-standers who have made them during the induction period on the assumption that third stage has been attained. Comments concerning the patient should be withheld until one is certain that the patient has lost consciousness and is irresponsive

## Stage III—Surgical Anesthesia

The third or surgical stage of anesthesia is characterized by loss of superficial reflexes The subject is no longer capable of voluntary movements Slight tapping on the eyelid no longer evokes the so-called 'lid reflex' The lid reflex" is not to be confused with the corneal reflex commonly employed by physiologists and pharmacologists as a guide to depth of anesthesia in laboratory animals The corneal reflex also is present in man and, as in the case of animals persists for some time as stage III is transcended It is not

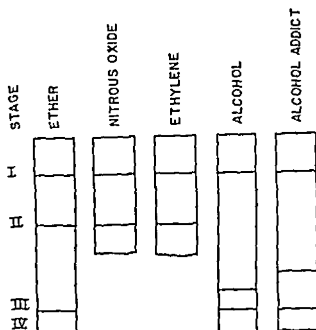



FIG 8 The variations in depth of the stages of anesthesia with different drugs With ether anesthesia the zone transcended in the third stage is comparatively wide allowing considerable latitude With alcohol the zone of third stage is narrow and passage from second stage is abrupt Second stage is a broad zone with alcohol With nitrous oxide and ethylene without anoxia the upper strata of the third stage is rarely transcended Chronic alcohol addicts manifest a narrow zone of third stage

a practical guide for depth of anesthesia because corneal ulcers often result from repeated touching of the cornea Respiration is rhythmical and resembles that noted in normal sleep Pulse and blood pressure, if elevated during stage II, return to pre anesthetic levels The third stage is broad and therefore is subdivided into substages referred to as planes Planes of anesthesia are designated by arabic numerals Depth of anesthesia is usually indicated as stage III plane 1, stage III plane 2, or stage I and stage II and so on

The *first plane* is characterized by a loss of superficial reflexes but little or no loss of muscle tone Occular movements continue The eyeballs oscillate rhythmically in a horizontal plane, when the lids are retracted and light enters the pupil As *plane 2* is traversed, occular movements cease, because the smaller muscles throughout the body including the oculo motor group lose their tone The pupils appear centrally fixed and constricted, but they continue to react to light The character of respiration is altered little in the first and second planes using most anesthetics, because the intercostal muscles and the diaphragm remain active Respiration remains rhythmical, changing little from plane 1 Inspiration and expiration are of equal duration Operations requiring pain relief only may be performed using first plane anesthesia Surgery requiring a moderate loss of muscle tone may be performed with second plane anesthesia As *plane 3* is transcended, a loss

of intercostal activity occurs Respiration becomes diaphragmatic in quality—inspiration is quickened and expiration is prolonged Muscle tone is considerably diminished Moderate dilatation of the pupils may occur The corneal reflexes are obtunded or abolished and secretion of tears ceases A quickening of the pulse rate and a slight fall in blood pressure are noted, but as a rule the circulatory changes are not remarkable at this point Surgery necessitating loss of tone of the larger muscles is performed with ease Relaxation of large muscles and loss of reflexes gradually appear as *plane 4* is reached Diaphragmatic activity is diminished, the pupils become widely dilated, and respiration is entirely diaphragmatic Inspiration is quickened and jerky, expiration is prolonged, and minute volume exchange is markedly diminished

## Stage of Medullary Depression

As stage IV is reached the medullary centers become depressed and ultimately inactive The respiratory center is the first of the medullary centers to become inactivated Respiratory efforts cease and unless artificial respiration is instituted promptly the patient dies The vasomotor center usually fails after the respiratory center The blood pressure falls the pulse may be quickened or slowed depending upon the drugs used and the status of the patient The heart continues to beat after respiratory efforts cease until the depressant effects of anoxia ensue Other drugs, chloroform for example, depress the circulatory and respiratory system simultaneously

A number of other important reflexes disappear as anesthesia is deepened The cough reflex disappears at the transition between stage II and III The vomiting and "gag" reflex disappear at the same time Tracheal and bronchial reflexes disappear in plane 2 or 3 Reflexes initiated by traction on the mesentery of an abdominal organ or upon the thoracic viscera disappear in plane 3 but may persist even into plane 4

## Recovery

When the anesthetic is discontinued recovery occurs in the reverse order After a long ether anesthetic the order of return of reflexes is variable

The signs of anesthesia enumerated in the foregoing paragraphs apply to ether Except for minor variations to be described under the discussion of individual drugs these signs are also applicable to the other currently employed volatile anesthetics Anoxia carbon dioxide excess heavy sedation basal narcosis with non volatile drugs modify and invalidate these signs These signs tend to vary with the extremes of age They are not satisfactory guides for determining the depth of hypnosis or basal narcosis with barbiturates and other non volatile drugs The signs are nullified if inhalation anesthesia is combined with basal narcosis with barbiturates or other non volatile drugs

## REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 16

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 pp 52–56

GILLESPIE N A Signs of anesthesia *Anesth & Analg* 22 275 1943

GUEDEL A E *Inhalation Anesthesia* New York Macmillan 1950

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SEEVERS M H The narcotic properties of carbon dioxide *New York State J Med* 44 597, 1944

SEEVERS M H and WATERS R M Pharmacology of anesthetic gases *Physiol Rev* 18 447, 1938

# NITROUS OXIDE

## Description

Nitrous oxide or nitrogen monoxide, as it is called is a stable, sweet smelling inorganic gas possessing a mild narcotic potency When clinicians speak of "gas" as an anesthetic, reference is being made to nitrous oxide Nitrous oxide is non irritating and easily inhaled Induction is rapid (two to three minutes), uneventful, and without struggling There is little or no irritation of the salivary and mucous glands of the upper and lower respiratory tracts Anesthesia is therefore devoid of troublesome secretions

## Potency

Nitrous oxide is a potent analgesic but a weak anesthetic Inhalation of a 20 per cent mixture with oxygen or air induces analgesia comparable to that obtained with 15 mgm of morphine Inhalation of an approximately 60 per cent mixture causes unconsciousness Surgical anesthesia is obtained with difficulty, unless alveolar concentrations of 80 per cent or upward are attained Herein lies the hazard of nitrous oxide for surgical anesthesia The physiologic limit of oxygenation is often exceeded in attempting to obtain *surgical anesthesia* (Fig 9) Surgical anesthesia below first plane is rarely

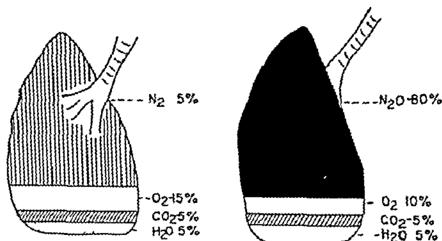



FIG 9 (A) The percentage composition of the gases in the alveoli at rest at ordinary atmospheric pressure (B) The percentage composition of the alveolar gases of a patient who requires an 80 alveolar concentration of nitrous oxide at ordinary atmospheric pressure in order to attain surgical anesthesia It is assumed all the nitrogen has been eliminated and replaced by nitrous oxide It can be seen that even under such circumstances a reduction in oxygen tension occurs Dilution of the nitrous oxide with nitrogen occurs at the expense of oxygen and obviously further enhances the already existing sub oxygenation The semi-closed system must be used to induce nitrous oxide anesthesia in order to wash out the nitrogen

IV

# GASEOUS ANESTHETICS

The gases are inorganic or organic substances Organic gases known to possess anesthetic qualities are hydrocarbons, halogenated hydrocarbons or ethers Xenon, nitrous oxide and carbon dioxide are the only inorganic gases possessing any notable anesthetic properties Nitrous oxide is still widely used in clinical medicine Carbon dioxide is merely of academic and historical interest Its use in anesthesia in most cases constitutes abuse Nitrogen is mildly narcotic under several atmospheres of pressure and is therefore of no importance Xenon is, at the present time, a pharmacologic curiosity and has been used in man to a limited extent The only suitable organic gases are either aliphatic or cyclic hydrocarbons None of the saturated hydrocarbons such as methane, ethane, propane and so on is suitable Unsaturation of aliphatic hydrocarbons enhances narcotic potency Ethane, for example, is practically devoid of anesthetic properties, whereas its unsaturated counterpart, ethylene, is a most suitable anesthetic

Increasing the molecular weight of a hydrocarbon increases its narcotic potency Seventy to 80 per cent ethylene yields satisfactory surgical anesthesia, compared to 40 per cent for propylene and 20 per cent for butylene The depth of anesthesia obtained with propylene is greater than that of ethylene Increasing the degree of unsaturation also influences narcotic potency Acetylene, which possesses a triple bond, is more potent than ethylene which has a double bond The cyclic arrangement of carbon atoms also influences potency Cyclopropane which has a cyclic configuration is a potent anesthetic in contrast to propane, the straight chained counterpart which is almost devoid of anesthetic properties

Propylene and acetylene enjoyed limited periods of popularity as anesthetics, but soon yielded their places to cyclopropane Ethylene, a most suitable anesthetic, is still used, except in communities where hospital authorities forbid the medical profession to do so because they are fearful of the fire hazard involved Cyclobutane has been investigated by Krantz and other workers It appears to possess pharmacologic and anesthetic properties similar to cyclopropane, but it is used little, if at all Three gases, then, are used in present day anesthesia practice nitrous oxide, ethylene, and cyclopropane These will be discussed in detail subsequently


REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 pp 21–30

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 pp 22–100

attained in healthy, vigorous subjects without some sub oxygenation The muscle relaxation is inadequate for most surgical procedures The gas is useful for procedures requiring abolition of superficial reflexes without muscle relaxation

## Systemic Effects

Pharmacologically nitrous oxide is an innocuous substance Few, if any, physiologic disturbances occur when nitrous oxide is administered *without anoxia* The respiratory system, the circulatory system including the heart, conductive tissues and blood vessels, the liver, the kidneys, the gastro intestinal tract, and other organs are not significantly affected However, instances in which anesthesia is obtained without some anoxia are infrequent Ordinarily the anesthetist is compelled to employ mixtures in which oxygen concentrations are too low for safety The majority of central nervous system depressants when given to excess cause death by asphyxia following paralysis of the respiratory center Overdosage causing medullary paralysis (with adequate oxygenation) is a remote possibility with nitrous oxide A mixture of 80 per cent nitrous oxide and 20 per cent oxygen at 3 atmospheres pressure is lethal to mice A lethal concentration in blood can only be attained administering the gas under a pressure of several atmospheres At atmospheric pressure the amount is far below the lethal dose The notion that nitrous oxide possesses no narcotic action, and that its effect is the result of anoxia, is not correct Fatalities during nitrous oxide anesthesia are the result of anoxia (anoxic anoxia) Fatalities are more frequent than is realized, despite the oft made statement that nitrous oxide is "safe"

Nitrous oxide anesthesia administered with adequate concentrations of oxygen differs physiologically and pharmacologically from that accompanied by anoxia The signs, symptoms, and effects of anoxia accompanying nitrous oxide anesthesia are no different than those noted with anoxia from other anesthetics It appears worthwhile, therefore, to briefly outline the symptoms and sequelae of anoxia during nitrous oxide anesthesia

## Anoxia During Anesthesia

Three phases of anoxia are recognized during nitrous oxide anesthesia—a precrisis, a crisis, and a terminal The *precrisis phase* is entered as the oxygen content is reduced below normal, and persists until the blood oxygen content is 12 volumes per cent A quickening of the pulse and an elevation in blood pressure characterizes this phase Respiration is stimulated, the rate being affected more than depth Presumably this is caused by reflex effects originating in the sino aortic chemo receptors The *crisis phase* is entered as the blood oxygen content falls below 12 volumes per cent, and persists until the reduction is 9 volumes per cent The elevation in blood pressure, due to stimulation of the vasomotor center via the sino aortic

mechanism, is pronounced The pulse, due to vagal stimulation slows to 60, 50 or even less Sectioning the vagi or the administration of anticholinergic drugs or barbiturates, which depress the cardiac portion of the vagus, abolishes or prevents the bradycardia The quickening of the pulse during the precrisis phase is the result of sympathetic stimulation The pupils dilate, cyanosis of a dark, inky, blue black hue appears Respiration becomes gasp ing and stertorous Twitchings of the small muscles first appear, these are followed by hypertonia, and a merging into convulsive movements Two factors are probably responsible for these neuromuscular responses (1) The effect of anoxia on the cortical and sub cortical cells, and (2) the tetany due to an alkalemia resulting from hyperventilation, which depletes alveolar carbon dioxide The neuromuscular phenomena are more pronounced when anoxia is induced with nitrogen than with depressant drugs Anesthetics "soften" and often completely prevent the convulsions

The climax or the third or terminal stage is reached, when the oxygen content falls below 9 volumes per cent to approximately 4 volumes per cent or less The medullary centers are depressed by the anoxia Respiration ceases, the blood pressure falls, and asystole then follows from direct depression of the myocardium Asystole occurs more frequently than ventricular fibrillation, although either may occur *A markedly slow pulse occurs before asystole* Obviously bradycardia during nitrous oxide anesthesia is an ill omen As a matter of fact any bradycardia during anesthesia, irrespective of the drug used, merits investigation

## Pathologic Effects of Anoxia During Anesthesia

The sequelae of even brief periods of anoxia may be disastrous The cere brospinal axis, particularly the phylogenetically newer portions, undergo irreparable damage when subjected to even brief periods of anoxia Few if any gross changes are found on post mortem examination when death occurs during a bout of asphyxia Petechial hemorrhages over the brain and serous surfaces are the only notable changes found Patients may survive resuscitation only to succumb after several hours The symptoms before death vary, depending upon the duration of anoxia Usually the patient re mains comatose after the mishap Dilated, sometimes unequal, pupils with or without nystagmus may be present Signs of cortical irritation, manifested by spasticity and convulsions, may be present The breathing becomes ster torous and the pulse bounding Later signs of upper motor neuron injury appear such as positive Babinskis The coma deepens, circulation fails, and a hyperthermia develops The temperature may rise to 107 108°F before death Post mortem examination of the brain reveals widening of the pericel lular and perivascular spaces due to edema If the survival period extends over several days, more specific changes develop Areas of necrosis, distrib uted through various portions of the brain, are common The cerebral cor

tex is most frequently the site of such changes, but the basal ganglia and the cerebellum may also be involved Once a neuron is devitalized, it never regenerates A transient swelling of the cytoplasm, with dissolution of the nuclear elements, occurs in the neurons This may be followed by a restitution to normal rather than by necrosis The fact that some patients manifest signs of severe central nervous system damage, but recover completely in due time, is explained by this fact Others are permanently afflicted because the cells become necrotic and die The necrotic areas are replaced by scar tissue The response or tolerance to anoxia is variable

Some patients who are anoxic following respiratory failure for considerable time have been none the worse for their experience In these instances respiratory failure without circulatory failure occurs The blood continues to circulate through the brain and despite its low oxygen content, some degree of oxygenation is maintained In other patients, a brief episode causes death In these instances, circulatory collapse promptly follows or accompanies respiratory failure It cannot be emphasized too strongly that successful resuscitation following combined circulatory and respiratory failure is invariably followed by serious and usually permanent damage to the nervous system If the cerebral circulation is interrupted for more than two or three minutes the patient dies from cerebral damage or, if he survives, he has permanent neurologic changes This commonly occurs after successful cardiac resuscitation

The neurologic sequelae following recovery from anoxia are varied They range from minor impairment of mental faculties to almost complete deterioration In addition blindness deafness, palsies Parkinsonism, and spasticity of various muscle groups remain as residual findings The types of neurologic complications which follow depend upon the site of the damage to the central nervous system Despite enthusiastic reports concerning cardiac resuscitation, which have appeared in the current medical literature the results are disappointing unless asystole is promptly recognized and cardiac massage is instituted immediately Cerebral damage is the rule rather than the exception

## Systemic Changes Caused by Anoxia During Anesthesia

A thick, glary mucus scant but sufficient in amount to cause vexsome obstruction and laryngeal spasm is often secreted during anoxia The intracranial pressure is markedly elevated a point of importance during intracranial surgery Serious metabolic disturbances accompany even mild degrees of anoxia Initially an alkalemia develops as a result of forced ventilation accompanying the anoxia The hyperventilation causes a reduction in carbon dioxide tension After a brief period acidosis ensues due to the accumulation of fixed acids, particularly lactic and phosphoric which accumulate due to the suboxygenation Carbohydrate metabolism is disturbed Sympathetic stimulation causes depletion of epinephrine in the adrenal gland Liver glyco

gen is mobilized as a result of the sympathetic stimulation, causing an elevation in blood sugar, the degree of which depends upon the severity of the anoxia and the glycogen content of the liver. Various functions of the liver are disturbed by anoxia. Bromsulfalein excretion, the most widely studied function during anesthesia, is impaired for 24 hours or more following brief periods of mild degrees of anoxia. Secretion of bile, the formation of bile salts, and various synthetic processes undertaken by the liver may be retarded during and following anoxia. Elevation in blood pressure, depression of cardiac muscle, constriction of the spleen, and an increase in capillary permeability are other derangements of importance caused by anoxia.

## Non Asphyxial Nitrous Oxide Anesthesia

Rarely can nitrous oxide be administered without anoxia, if used alone with oxygen. By combining nitrous oxide with another inhalation anesthetic such as vinyl ether, ethyl ether, chloroform or trichlorethylene, an additive effect is secured. An additive effect is also obtained by combining the gas with non volatile basal narcotics. Tribromethanol, morphine, meperidine, and ultra short acting barbiturates are suitable for this purpose. Combining the drugs permits reduction of the nitrous oxide tension necessary for surgical anesthesia. The oxygen tension may then be increased to the physiologic level and the hazard of anoxia is thereby lessened. Muscle relaxants may be added when muscle relaxation is desired. The combination of thiopental, nitrous oxide, and curare is currently popular. The curare is non analgesic but provides relaxation which neither the barbiturate nor the nitrous oxide can provide. The nitrous oxide provides analgesia which neither the thiopental nor the curare can provide.

## Contraindications to Nitrous Oxide

Obviously then, unless administered in non asphyxial concentrations, nitrous oxide is contraindicated whenever *the slightest degree of suboxygenation* would be a hazard. Its use in the presence of cardiovascular disease, shock, liver disease, pulmonary insufficiency, anemia, and so on is not without hazard unless adequate oxygenation is assured. When adequate oxygenation is assured there is no contraindication to nitrous oxide.

## Use in Negroes and Heavily Pigmented Patients

The belief that negroes do not tolerate nitrous oxide has no scientific basis. Anesthetists who rely entirely upon cyanosis as a guide to the degree of oxygenation during anesthesia invite disaster. Cyanosis does not appear until a severe degree of anoxia is present in anemic subjects. In fact it may not appear at all. Likewise in thick skinned individuals or those who are heavily pigmented cyanosis is difficult to discern. Obviously, the hazard of asphyxia is greater in negroes or other heavily pigmented persons unless one is unduly cautious.

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concentrations of 50-60 per cent greater degrees of analgesia are obtained. Approximately 60 per cent in the inhaled mixture causes unconsciousness. In most instances 75 to 80 per cent in the alveoli is sufficient to establish and maintain surgical anesthesia. Induction, as in the case of nitrous oxide, is rapid requiring two to three minutes. Recovery, likewise, is rapid. Almost complete elimination occurs within three to four minutes. Nausea and vomiting more frequently follow ethylene than nitrous oxide. The depth of anesthesia is somewhat more profound with ethylene than with nitrous oxide. In elderly, less resistant, and well premedicated subjects, lower second plane anesthesia, with some degree of muscle relaxation, may be attained. Ordinarily lower first plane anesthesia is obtained without anoxia. Less difficulty is experienced by beginners in anesthetizing patients with ethylene than with nitrous oxide because of this somewhat greater potency.

## Systemic Effects

Ethylene, like nitrous oxide, causes no noteworthy systemic disturbances. Respiratory paralysis from overdosage does not occur when oxygenation is adequate. As is the case with nitrous oxide, only under increased pressure of several atmospheres may lethal amounts be dissolved in the tissues. Obviously this cannot happen clinically. Fatalities, as in the case of nitrous oxide, result from anoxia when the oxygen tension is reduced below safe limits. Ethylene possesses a wider margin of safety than nitrous oxide, because the alveolar oxygen tension during surgical anesthesia can be maintained within normal physiologic limits.

## Anoxia During Ethylene Anesthesia

The immediate, delayed, and remote effects of anoxia induced by inhaling asphyxial concentrations of ethylene are exactly the same as those of anoxia during nitrous oxide anesthesia. The inky, black cyanosis characteristic of anoxia during nitrous oxide anesthesia is not seen during ethylene anesthesia. A gray cyanosis appears instead. Presumably there is difference in the calibre of the cutaneous vessels being greater during nitrous oxide anesthesia than ethylene.

## Flammability

The flammability of ethylene limits its usefulness as an anesthetic, particularly in localities where humidity is low and static electricity is a problem. The limits of flammability in oxygen at ordinary room temperature and atmospheric pressure is 3-85 per cent. One is, therefore, dealing with explosive mixtures when the gas is used for either analgesia or anesthesia.

## Uses

Ethylene may be used for the same purposes as nitrous oxide. Ethylene is excellent as a preliminary to ether and is largely used for that purpose.

### Uses of Nitrous Oxide

Nitrous oxide is used chiefly for induction of ether anesthesia, as a sole anesthetic for minor surgical procedures not requiring relaxation, for operations in which a fire hazard exists, and for analgesia in obstetrics and dentistry Nitrous oxide combined with oxygen is not flammable Until a more potent, safe, non flammable, inhalation anesthetic is discovered, nitrous oxide will continue to be used in combination with non volatile drugs, when a fire hazard exists Nitrous oxide supports combustion Mixtures of nitrous oxide and ether, vinyl ether, cyclopropane, or other flammable anesthetics ignite and continue to burn because nitrous oxide readily yields its oxygen atom to support combustion

Concentrations of 50 or 60 per cent nitrous oxide with oxygen, inhaled intermittently, provides excellent analgesia Its pleasant odor, its non irritating effects, and its freedom from postoperative nausea and vomiting make it an ideal drug for this purpose

### REFERENCES


ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield, Thomas 1953 p 21

ADRIANI, J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 70

ADRIANI J *The Chemistry of Anesthesia* Springfield Thomas 1946 p 62

CLEMENT F *Nitrous Oxide Anesthesia* Philadelphia Lea & Febiger 1952

COLLINS V J *Principles and Practice of Anesthesiology* Philadelphia Lea & Febiger 1952

COURVILLE C B and BATTEN C T Mental disturbances following nitrous oxide anesthesia *Anesthesiology 1* 261–273 1940

COURVILLE C B *Untoward Effects of Nitrous Oxide Anesthesia* Mountain View Calif Pacific Press Publishing Association 1939

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941

SEEVERS M. H. and WATERS R. M Pharmacology of anesthetic gases *Physiol Rev 18* 447 1938

SEEVERS M H BENNETT J H. POLL H. W *et al* Analgesia produced by nitrous oxide ethylene and cyclopropane in normal human subjects *J Pharmacol & Exper Therap 59* 291 1937


## ETHYLENE

### Properties

Although pharmacologically ethylene and nitrous oxide are similar, significant differences do exist between them Chemically ethylene is an unsaturated stable hydrocarbon possessing an ethereal odor It is the simplest member of the olefin series The odor is unpleasant to many patients but the sense of smell is soon obtunded and since it does not possess any irritating properties, patients cease to resist it after the first or second breath Ethylene is somewhat more potent than nitrous oxide Usually 20 to 25 per cent with oxygen induces analgesia of similar intensity to that of nitrous oxide In

dose is wide Unlike the situation with nitrous oxide and ethylene, it is not necessary to "wash out" the nitrogen from the inhaler to induce and maintain anesthesia (Fig 10) Therefore, the closed system with rebreathing may be used at the outset Anoxia is not a factor as in the case of nitrous oxide and ethylene

Cyclopropane is considered a "major" anesthetic drug Anesthesia may descend through stage III and into stage IV Respiration fails before circulatory collapse occurs The heart continues to beat for sometime after respiratory failure from overdosage The chances of resuscitation are good in the event of overdosage, provided the anesthetist is alert Muscle relaxation is adequate for major surgery in approximately 90 per cent of cases in the hands of experienced administrators Where it is not adequate, muscle *relaxants are used as adjuncts in lieu of deep anesthesia*

## Induction and Recovery

Induction of anesthesia is rapid, consuming two to three minutes Recovery likewise is rapid The bulk of the gas is eliminated unchanged through the lungs within 10 minutes Minute traces continue to circulate in the blood for several hours after anesthesia has been discontinued This is due to the slow release of the gas, which has been absorbed by the lipoid tissue

## Effects on Respiration

Cyclopropane like nitrous oxide and ethylene, causes few derangements of physiologic functions Irritation of the respiratory tract is uncommon, unless inhaled concentrations exceed 50 per cent Salivation and secretion of mucus, likewise, are uncommon Depression of respiration, particularly in the lower planes, is frequent but does not occur in all cases There is a decrease in both depth and rate of respiration The minute volume exchange is reduced but not to the point of affecting oxygenation of the blood Arterial blood oxygen content remains unchanged or is slightly elevated The venous blood oxygen is increased, the blood becomes "arterialized" Whether or not this is the result of increased blood flow or decreased utilization by the tissues, or both is undetermined The bright red appearance of the blood has given rise to the misconception that cyclopropane permits better oxygenation than other anesthetics Less oxygen is present in the inhaled mixture when cyclopropane is used than with ether Four per cent ether is necessary for surgical anesthesia Thus as much as 96 per cent oxygen may be administered with ether Twenty per cent cyclopropane is necessary for anesthesia Thus only 80 per cent oxygen is the allowable average

## Respiratory Acidosis and Shock

The diminished ventilation results in a *respiratory acidosis* Both alveolar carbon dioxide and blood carbon dioxide tensions are elevated At the con

Satisfactory anesthesia is obtained if combined with a basal drug such as avertin, ultra short acting barbiturates, or a combination of morphine and scopolamine It is possible to use ethylene alone for major surgery in old patients, but as a rule the drug must be fortified with ether or, be supplemented with an adjunct, such as curare, to obtain muscle relaxation

### REFERENCES


ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas, 1953 p 24

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 77

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941

SEEVERS M H and WATERS R M Pharmacology of anesthetic gases *Physiol Rev* *18* 447 1938

SEEVERS M H BENNETT J H POHLE H W *et al* Analgesia produced by nitrous oxide ethylene and cyclopropane in normal human subjects *J Pharmacol & Exper Therap* *59* 291 1937


## CYCLOPROPANE

### Description

The discovery of the anesthetic properties of ethylene, by Luckhart in 1923, prompted the investigation of the next higher molecular weight, unsaturated hydrocarbon in the olefin series, propylene Studies of propylene led to the investigation of its isomer, cyclopropane, which occurred as an impurity in propylene Cyclopropane is a saturated, cyclic hydrocarbon It is a colorless, flammable gas possessing a sweet, rather pleasant odor The gas is heavier than air, liquefies at 75 pounds pressure at room temperature, and is stable under ordinary conditions of storage

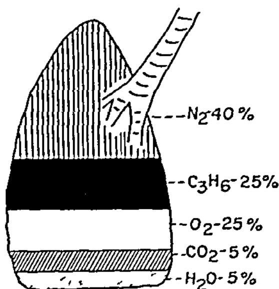



Fig 10 The percentage composition of gases in the alveoli during cyclopropane anesthesia It is possible to administer more than 20 per cent oxygen with the cyclopropane The nitrogen need not be "washed out" Anoxia in contra-distinction to nitrous oxide and ethylene is not a factor during cyclopropane anesthesia

### Potency

Cyclopropane possesses greater potency than ethylene or propylene Analgesia is obtained by inhaling a 4 5 per cent mixture A 7 10 per cent mixture causes unconsciousness Surgical anesthesia is obtained when concentrations ranging from 12 20 per cent are inhaled Respiratory failure occurs with a 40 per cent concentration The margin of safety between the anesthetic and lethal

proved when anoxia exists. No histologic changes are caused by cyclopropane and no persistant functional disturbances remain after removal of the drug. This irritability of conducting tissues by cyclopropane is enhanced by the simultaneous administration of sympathomimetic amines. Epinephrine is the most dangerous of this group of amines, giving rise to serious arrhythmias, particularly ventricular tachycardia and ventricular fibrillation. Other pharmacologically and chemically related amines behave similarly, but the disturbances are not as serious nor as frequent. Procaine and procaine amide (*pronestyl*) have been suggested as prophylactic agents to prevent or

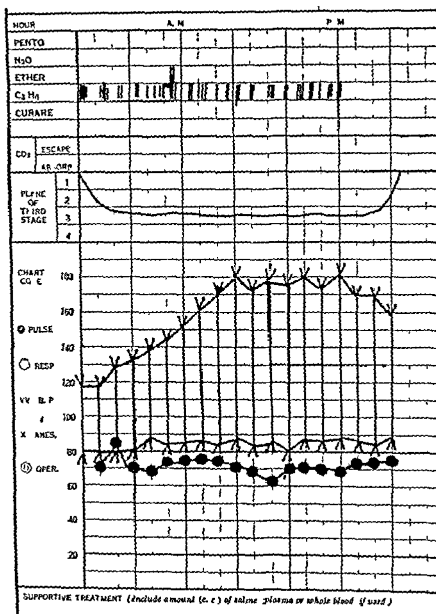



FIG. 11. Graph showing the elevation in blood pressure occasionally encountered during cyclopropane anesthesia. Note the pulse rate is unchanged and pulse pressure is widened.

clusion of anesthesia, a hypotension is occasionally noted which has been referred to as "cyclopropane shock." Carbon dioxide retention is believed to be the causative factor. Locally, carbon dioxide causes a vasodilatation while centrally it stimulates the vasomotor center. At the conclusion of anesthesia the central effects disappear as the carbon dioxide is eliminated, but the local effects persist. This may be the cause for the hypotension.

## Effects on Bronchi and Larynx

Laryngeal and bronchial spasm are more frequent during cyclopropane anesthesia than with other inhalation anesthetics. Some believe these effects to be due to a parasympathetic stimulation caused by the drug. This is the basis for the contention that cyclopropane should not be used for patients who have bronchial asthma.

## Effects Upon the Circulatory System

Circulatory disturbances during cyclopropane anesthesia are of considerable concern, and often preclude its use in patients with heart disease. The effects of cyclopropane upon the myocardium and cardiac output have not been studied in any great detail in man. In animals, little or no depression of the myocardium occurs until the deeper planes of anesthesia are attained. Clinical experience suggests that the heart muscle is depressed little, if at all, in the lighter planes of anesthesia and that there is no significant reduction in cardiac output.

*The most profound effects are on the automatic or conducting tissues.* Increased irritability occurs, giving rise to arrhythmias. The effects of cyclopropane on cardiac rhythm have been the subject of considerable research in both man and animals. A slowing of the pulse invariably occurs. The rhythm remains regular. This bradycardia is usually vagal in origin. However, *more serious changes in cardiac rhythm occasionally occur.* Evidence exists that the sympathetic nervous system receptors in the splanchnic area are stimulated by cyclopropane. These impulses are then relayed to the hypothalamic centers via the sympathetic pathways and thence to the heart via the cervical sympathetics. The conducting tissues are sensitized reflexly and their irritability is enhanced greatly. Arrhythmias are not peculiar to cyclopropane alone. Arrhythmias may arise during anesthesia with any anesthetic drug under many circumstances. In most cases, they are supraventricular in origin. During cyclopropane anesthesia, however, the pacemaker shifts even below the auricle. Arrhythmias of ventricular origin are possible. A. V. nodal rhythm, ventricular premature beats, and ventricular tachycardia are observed. Ventricular fibrillation can occur if irritability is marked. Arrhythmias are seen most frequently during deep anesthesia, when ventilation is poor, and in patients with heart disease. The cardiac effects of cyclopropane are purely functional. Arrhythmias disappear as anesthesia is lightened, if the drug is withdrawn, and if oxygenation is im

the anti diuretic hormone of the pituitary during anesthesia An increase in tubular reabsorption occurs Other factors contributing to this change are alterations in blood volume, changes in blood flow through the kidney, decreased absorption of fluid and fluid loss by sweating, and so on

## Effects on Smooth Muscle

Gastro intestinal motility and tone is decreased even in the light planes of anesthesia Peristalsis is decreased progressively as anesthesia deepens Uterine motility, likewise, is decreased as anesthesia deepens The gas passes into the fetal circulation After 15 minutes, maternal arterial blood and fetal arterial blood contain approximately the same amounts of cyclopropane The new born is narcotized as with other anesthetics Recovery time, however, is shorter when cyclopropane has been used for delivery than when ether or non volatile drugs are used, and longer than when ethylene or nitrous oxide are used It is not uncommon for laryngeal spasm to develop, when resuscitation is attempted after delivery with cyclopropane This occurs particularly when instrumentation with catheters, laryngoscopes, and suction tubes is attempted The tracheal reflex appears more active than usual The spleen does not constrict but often dilates during cyclopropane anesthesia

## Appearance During Anesthesia

The skin assumes a ruddy red color Sweating is uncommon during cyclo propane anesthesia It differs from ether in this respect The skin tempera ture rises due to dilatation of the peripheral vessels The temperature regu lating center is depressed Body temperature usually falls but varies with environmental temperature If the room is hot, the temperature may rise above normal

## Uses

Cyclopropane is suitable for minor and major surgery Muscle relaxation satisfactory for major surgery cannot be always obtained without resorting to depths of anesthesia which cause disturbances in cardiac rhythm The muscle relaxants are used as adjuncts or ether is added to fortify the mixture to avoid deep anesthesia

Cyclopropane is preferred to other forms of general anesthesia because of the ease and pleasantness of induction, the rapid return of reflexes during recovery, and the controllability of depth during the maintenance phase A "quiet abdomen" and thorax is necessary to perform intra abdominal and intrathoracic surgery The rate and depth of respiration are invariably de creased during cyclopropane anesthesia The quiet breathing affords ideal operating conditions At times respiration is so shallow that it must be augmented by inflating the lungs intermittently by compressing the breath ing bag This is referred to as *assisted respiration* Apnea, particularly when morphine is used, is common, necessitating artificial or *controlled respiration*

reduce the frequency of cardiac disturbances These substances depress the heart There is no agreement concerning their efficacy in overcoming arrhythmias, and their routine use during cyclopropane anesthesia is not advised The policy of adding a second dangerous drug to make one which is potentially dangerous, safer, does not appear rational Invariably, the addition of ether to the inhaled mixture causes these arrhythmias to disappear in man, provided the airway is unobstructed

An elevation in blood pressure is not uncommon during cyclopropane anesthesia Exactly how it comes about is undetermined Some feel that it is due to the respiratory acidosis and to the increase in blood carbon dioxide tension It occurs more frequently in normotensive subjects who manifest a respiratory depression (Fig 11) The rise in the systolic phase may be as much as 60 or 70 mm Hg The rise in blood pressure in hypertensive subjects may not be as pronounced, but does cause concern when severe hypertension exists When a notable rise occurs, it is advisable to discontinue the drug in hypertensive subjects The hypertension does not persist after anesthesia is discontinued Assisted respiration often causes a reduction in blood pressure, but does not prevent or eliminate the hypertension completelv At times the pressure returns to normal and then falls to sub normal levels passing into the state referred to, erroneously, as "cyclopropane shock"

A reduction in blood and plasma volumes, together with an increase in hematocrit values, is observed but is not as significant or as pronounced as it is with ether or chloroform Bleeding appears to be increased during cyclopropane anesthesia more so than when other agents are employed This is apparently due to a capillary or arteriolar oozing which results from a combination of two factors an increase in blood pressure, and dilatation of the peripheral vessels, particularly the capillaries No significant alteration in bleeding or clotting time occurs The oozing ceases upon closure of the wound *Although it is more frequent and pronounced during cyclopropane* anesthesia, this phenomenon is not limited to cyclopropane alone Increased bleeding also occurs during ether or ethylene anesthesia, and during narcosis with thiopental

## Metabolic Effects

No metabolic disturbances of any consequence are noted during cyclopropane anesthesia Alterations in total base, plasma carbon dioxide combining power, and blood glucose are not clinically significant Liver function measured by the bromsulfalein excretion, is not affected

A suppression of urinary output, characteristic of most forms of anesthesia and basal narcosis, also occurs during cyclopropane anesthesia The nitrogenous elements of the blood rise during anesthesia A compensatory polyuria follows in the recovery period A return of the urea nitrogen to normal follows conclusion of anesthesia The oliguria is due in part to a liberation of

PRICE H L CONNER E. H, DRIPPS R D Concerning the increase in central venous and arterial blood pressure during cyclopropane anesthesia in man *Anesthesiology* *14* 1-9 1953

REID C Anesthesia in relation to cardiac di ea e *Anesthesiology* *2* *161* *1941*

ROBBINS B H *Cyclopropane Anesthesia* Baltimore Williams and Wilkins 1940

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STORMONT H R. HATHAWAY, F E., SHIDEMAN F E. and SEEVERS, M H. The acid b e balance during cyclopropane anesthesia. *Anesthesiology* *3* 369-3/8 1942

STUTZMAN J W ALLEN C R and MEEK W J The prevention of cyclopropane epi nephrine tachycardia by di-ethyl ether *Anesthesiology* *3* *259* 1942

STUTZMAN J W, ALLEN C R and MEEK W J Response to the digitalized heart to cyclopropane and epinephrine. *Anesthesiology* *3* 644-649 1942

TAYLOR I B Cyclopropane anesthesia *Anesthesiology,* *2* 641, 1941

Apnea is deliberately induced at times to facilitate certain intra thoracic or intra abdominal manipulations

## Controlled Respiration

Apnea for controlled respiration is more easily induced with cyclopropane than with ether The apnea results from a combination of three factors (1) Depression of respiration Morphine (used for premedication) decreases the sensitivity of the respiratory center to carbon dioxide Cyclopropane also depresses the respiratory mechanism (2) Hyperventilation removes carbon dioxide and decreases the tension necessary to stimulate the respiratory center (3) Over distention of the alveoli (by inflating the lungs with the gas mixture) stimulates the Hering Breuer reflex and inhibits inspiration The anesthetist then breathes at will for the patient This he may do at a time convenient to him from the standpoint of surgery

## Advantages of Cyclopropane

The absence of metabolic disturbances and the wide margin of safety are desirable factors The cardiac effects and its highly flammable nature are the two objectionable features of the gas Technically, cyclopropane is more difficult to administer than other anesthetics All patients anesthetized with cyclopropane do not follow similar patterns of behavior Half may follow a given general pattern, the remainder a bizzare pattern of reactions The administration of cyclopropane by individuals not familiar with its pharmacologic effects, or by those who do not possess the technical skill to administer the drug, has resulted in preventable deaths and unsatisfactory performances of the drug as an anesthetic All concentrations of cyclopropane used for analgesia and anesthesia are within the flammable range Cyclopropane must never be administered when a cautery, an electro surgical unit, or any other source of ignition is used during the operation

## REFERENCES

Acierno L J and DiPalma J R The effects of ether cyclopropane and chloroform on the isolated auricle of the cat. *Anesthesiology 12* 567–573 1951

Adriani J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 27

Adriani J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 86

Allen C R Stutzman J W Meek W J The production of ventricular tachycardia by adrenalin in cyclopropane anesthesia *Anesthesiology 1* 158–166 1940

Allen C R Stutzman J W Slocum H C and Orth O S Protection from cyclopropane epinephrine tachycardia by various drugs *Anesthesiology 2* 503–511 1941

Burstein C L Apnea during anesthe ia *Anesthesiology 2* 530–534 1941

Dripps R D The immediate decrease in blood pressure seen at the conclusion of cyclopropane anesthesia. *Anesthesiology 8* 15–31 1947

Goodman L and Gilman A. *The Pharmacological Basis of Therapeutics* New York Macmillan.

Meek W J Hathaway H R and Orth O S The effects of ether chlo oform and cyclopropane on cardiac automaticity *J Pharmacol & Exper Therap 61* 240 1937

PRICE H L CONNER E H, DRIPPS R D Concerning the increase in central venous and arterial blood pressure during cyclopropane anesthesia in man *Anesthesiology* *14* 1–9 1953

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# V

# VOLATILE LIQUIDS

The currently used volatile liquids suitable for inhalation anesthesia are ethers or halogenated hydrocarbons *Ethyl ether* remains the reliable standby of inhalation anesthesia *Vinyl ether* (Vinethene), the unsaturated counter part to ethyl ether is also currently used Numerous aliphatic ethers have been studied for anesthetic properties, but only ethyl ether and vinyl ether appear to have withstood the test of time Among those studied have been *cyclopropyl methyl ether* (Cryprome), *cyclopropyl ethyl ether* (Cypreth), and *methyl propyl ether* (Metopryl), an isomer of ethyl ether These have not been adopted because they have few or no advantages over ethyl or vinyl ether

Halogenation of a hydrocarbon increases the narcotic potency, decreases the volatility and reduces the flammability The cardiotoxic and hepatotoxic effects are enhanced Thus methane, which exhibits little or no narcotic potency, acquires anesthetic properties when chlorine is substituted for one hydrogen atom to form *methyl chloride* The potency is further increased when two hydrogen atoms are replaced to form methylene dichloride, and still more, when three hydrogen atoms are replaced to form *trichlormethane (Chloroform)* Replacement of the hydrogen atoms by four chlorine atoms yields carbon tetrachloride whose potency surpasses that of chloroform, but whose toxicity limits its clinical usefulness Replacement of a hydrogen atom of ethane by chlorine forms *ethyl chloride*

Chloroform and ethyl chloride are the most important drugs in the halo genated hydrocarbon group Methyl chloride and ethyl bromide have been but are no longer used clinically *Trichlorethylene* (trilene) is popular as an anesthetic and as an analgesic The halogenated derivatives which yield clinically useful compounds are derived from chlorine and bromine Suitable iodine or fluorine derivatives are unknown

The vapors of volatile liquids are effective at lower alveolar tensions than are the gases The effective alveolar tension of chloroform is 4 to 5 mm Hg, that of ether 30 to 55 mm Hg, that of vinyl ether 30 to 40 mm Hg, and that of ethyl chloride 40 to 50 mm Hg These tensions are low compared to those of cyclopropane (190 mm Hg) nitrous oxide (600 mm Hg), and ethylene (575 mm Hg) Apparatus for the administration of gases is more complex than that used for liquids The minimum requisites for administra tion of vapors are an open mask and air as a vehicle and source of oxygen The vapors of volatile drugs cause more pronounced effects on the respiratory tract than do the gases The term "irritation" is often used to describe the effects of the inhalants on the lung Actually, there is no damage whatever

to the lung parenchyma What is referred to as irritation is stimulation of the mucous glands and the vagal receptors in the lung The latter causes exaggerated respiratory movements

## ETHER

### Properties

In spite of numerous attempts to supplant ethyl ether, the drug remains an old standby and is the choice in cases of doubt The pungent, characteristic odor of ethyl ether is familiar to all clinicians and students of medicine and requires no description here

Ethyl ether is a clear, mobile flammable liquid which boils close to body temperature (36 C ) Anesthetic ether is made by interacting alcohol with sulphuric acid Ethyl alcohol, present in amounts up to 2 per cent, is actually a contaminant of manufacture The alcohol does no harm Removal of the alcohol entails considerable effort and accomplishes little more than to raise the cost of manufacture The alcohol is not a preservative as is erroneously believed by many students

### Effects of Impurities

Considerable nonsense has been written concerning the effects of impurities found in ether on the patient Fatalities due to thoughtlessness, improper technique, overdosage, and other causes have been blamed upon contaminants and impurities rather than faulty technique Ether is subject to slow oxidation in the presence of air or oxygen Peroxides form first Later, aided by the peroxides, the alcohol is converted to acetaldehyde Traces of aldehydes or peroxides have no apparent effect upon the safety and conduct of anesthesia Prolonged induction periods have been noted in dogs, when these impurities have been deliberately added to ether Ether peroxides are unstable and readily decompose They thus may contribute to the explosion hazard Ether may be stabilized by excluding oxygen from the sealed package or providing some method for its removal after the package is sealed Copper, iron, and other metals are preferentially oxidized when coated over the interior of the container The oxygen in the air which is sealed in the container, combines with the metal to form an oxide The ether remains unaltered for a long period of time in the oxygen free environment

### Potency and Safety

Surgical anesthesia is established when approximately 4 per cent (30 mm Hg tension) is present in the alveoli Approximately 8 per cent or (60 mm Hg tension ) causes paralysis of the respiratory center Ether, therefore, possesses a wide margin of safety There is a progressive depression of the cerebrospinal axis from above downward Respiratory failure,

V

# VOLATILE LIQUIDS

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cyclopropane, are absorbed by the "watery" tissues than is ether The air blood ratio (solubility coefficient) for ether is high compared, for instance, to cyclopropane (1 15 for blood) A high alveolar partial pressure is required for rapid saturation of blood The tissues are saturated slowly Once saturated and anesthesia is discontinued, desaturation is slow Each circuit of venous blood coming to the lungs from the tissues releases to the alveolar air 1 unit of ether for every 16 it holds The remaining 15 return once again to the peripheral capillaries With the next circuit the partition is again in the ratio of 1 15 and continues so with each succeeding circuit The circuit must be repeated many times before the bulk of the drug is eliminated In the case of cyclopropane, the ratio is reversed being 0 4 1 The amount retained is considerably less than that passing into the alveoli Fewer circuits are required for complete elimination The high coefficient of solubility of ether in blood and water favors a gradual slow saturation and desaturation of all tissues The longer the period of anesthesia, the greater is the amount of ether absorbed Recovery time is dependent upon duration and depth of anesthesia The tissues absorb ether in a sponge like manner, so to speak, but release it slowly Recovery following long operations performed with deep ether anesthesia, such as gastrectomies and colectomies for example, may require hours

## Effect on Respiratory System

Ether exerts a notable effect upon the respiratory system The mucous glands are stimulated and copious secretions develop, even though anti cholinergic drugs are used as inhibitors The salivary glands are stimulated during induction but they are depressed during the maintenance phase of anesthesia The secretions are mostly in the upper respiratory tract, where the mucous and salivary glands are most abundant Bronchorrhea is less pronounced Secretions are objectionable from three standpoints (1) They cause obstruction and impair ventilation (2) they help disseminate infection and (3) they cause blockage of the bronchi predisposing to atel ectasis An increase in depth of respiration occurs in the upper planes of the third stage It is believed this increase in minute volume exchange is caused reflexly by a local effect upon the vagal nerve endings in the alveoli There is no direct stimulation of the respiratory center by the drug The respiratory center is not depressed until the *fourth plane* or *fourth stage* is reached As the intercostal muscles become inactive the diaphramatic excursions are augmented to compensate for the inactivity Diaphramatic activity is reduced in fourth plane

Allusion is frequently made to the irritating affects of ether upon the lungs No histologic changes can be demonstrated in the mucous membranes of the bronchioles or alveoli during or after ether anesthesia Ether as well as other inhalation anesthetics do not cause pulmonary edema Pneumonitis

almost without exception, ensues before circulatory failure The blood concentration causing respiratory arrest is several times that which causes myocardial depression The possibility of resuscitation is greater after respiratory failure due to ether than it is with any other of the currently used volatile drugs Induction is prolonged and difficult It is more so with ether than with other inhalation anesthetics A number of factors are responsible for this The vapor is pungent The patient must become acclimatized to it by a gradual increase in concentration Abrupt increases in concentration initiate coughing and struggling This may be considered a safety factor because the patient, in a way, has something to say concerning the induction The drug cannot be administered faster than tolerated Fatalities from overdosage during induction are more frequent with rapid acting, non irritating drugs, such as cyclopropane, thiopental, and ethyl chloride, than with ether

## Induction of Anesthesia

Induction time, even when experts administer ether "straight," may be fifteen minutes or more The second stage is longer and more eventful than that of other anesthetics The unpleasantness of a "straight ether" induction lingers for a long time in the memory of many patients To avoid the unpleasantness and to shorten this stage, a rapid acting, nonirritating anesthetic, called the primary or induction agent, is used first When anesthesia is established with the primary agent, the ether is administered as rapidly and in as great a concentration as tolerated until the tension necessary to maintain surgical anesthesia is attained Then the primary agent is withdrawn Higher concentrations are tolerated at the outset using this technique Induction time is ½ to ⅓ that of "straight ether" Even though induction agents are used, the ether must be added gradually, otherwise coughing ensues Ethylene or nitrous oxide are used for induction in closed inhalers, vinyl ether is used for the "open drop" technique Chloroform and ethyl chloride may be used, but are avoided for the obvious reason that they disturb cardiac function Cyclopropane, avertin, and the short acting barbiturates are used, but are not wholly satisfactory because it is not always possible to avoid laryngeal spasm, coughing, or depressed respiration The discrete anesthetist prefers the gases or vinyl ether

## Absorption and Elimination

Ether undergoes no change in the body Elimination is largely by exhalation (90%) Some is eliminated in the urine sweat, tears, and gastrointestinal contents Ether is, comparatively speaking, soluble in water (6 parts per hundred, chloroform one part in 250) Tissues, regardless of lipoid content, absorb more ether than they do other volatile drugs Less of the lipophilic anesthetics of low water solubility, such as chloroform and

power Metabolic acidosis results The importance of the acidosis of ether anesthesia is open to question The acidosis is more pronounced and of greater severity in laboratory animals than in man The severity varies with conditions of surgery and anesthesia, notably depth, duration, and the presence or absence of hypoventilation A gradual return to the pre anesthetic state occurs during recovery, as the fixed acids are eliminated Although of no particular significance in the so called normal individual, this acidosis cannot be disregarded in patients with dehydration, nephritis, diabetes, and other situations accompanied by disturbances in acid base balance The relationship of acidosis to *ether convulsions* is discussed under the section on vinyl ether Total base and concentrations of various cations in blood are ordinarily not significantly altered by ether

## Effects on the Liver and Kidney

Certain liver functions are disturbed by ether anesthesia Bromsulfalein excretion and hippuric acid synthesis are impaired for a period varying from hours to days, depending upon the depth and duration of anesthesia Con comitant anoxia suppresses dye excretion still more Although urinary output is suppressed temporarily, no specific histologic changes can be demonstrated in the kidney Reduction in kidney function is transient Vasoconstriction of the efferent arterioles occurs, which influences renal function Evidence that ether damages or "irritates" the kidney of man is lacking The effect is purely functional As in the case of other anesthetics, the reduction in urinary output is due in part to release of the anti diuretic hormone from the pituitary gland

## The Effects on Smooth Muscle

Ether depresses smooth muscle of the gastro intestinal and genito urinary tracts Gastro intestinal tone, motility, and secretory activity are decreased or completely inhibited Uterine activity likewise is decreased The uterus is relaxed by deep ether anesthesia Labor is inhibited and halts completely as anesthesia deepens Ether passes through the placenta to the fetus Etherized mothers give birth to etherized babies As soon as the new born breathes, the ether is eliminated by exhalation The longer the anesthetic is administered prior to delivery, the more ether the fetus absorbs and the longer is the recovery period In this respect ether differs from ethylene and nitrous oxide, which are eliminated within several minutes

## Uses and Advantages

Ether provides adequate muscle relaxation for all types of major surgery When used with curare, a potentiating effect is noted The dose of curare must be reduced by approximately ⅓ in most instances Ether possesses a wide margin of safety, does not disturb the cardio vascular system, and may

in the postoperative period is not due to a direct effect of ether The role of ether in enhancing and disseminating infections, and in activating latent tuberculosis, is controversial Secretions favor the dissemination of infection from one part of the respiratory tract to another The initiation of an infectious process by ether is not likely Ciliary activity is decreased by all anesthetics, including ether This favors the inter mingling of the flora of the upper and lower respiratory tract Laryngeal spasm is not common in well conducted ether anesthesia, but is a frequent occurrence when inexperienced individuals attempt to administer ether Ether is a bronchodilator The dilatation is due to a direct depression of smooth muscle and to sympathetic nerve stimulation

## The Effects on the Circulatory System

Unlike cyclopropane, the cardiac effects of ether are not significant In perfusion experiments in vitro, the concentration necessary to depress the myocardium is approximately three times that which depresses the medullary centers Cardiac output is not decreased, more often, it is increased The pulse rate may be accelerated five to ten beats if it changes at all Arrythmias due to sensitization of the conducting tissues to epinephrine and related amines, characteristic of cyclopropane and chloroform, do not occur, or if they do occur, they are of little clinical significance Spontaneous arrythmias are uncommon during ether anesthesia When they occur, they are superventricular in origin, transient, and not serious Venous pressure is unchanged unless stage II is accompanied by excitement, at which time it is elevated The blood pressure varies little from the pre anesthetic level Contrary to the view expressed years ago, ether is not contraindicated in patients with cardiovascular disease As a matter of fact, it is the anesthetic of choice for major surgery in most instances Capillary permeability is increased by most anesthetic drugs, but more so by ether than by cyclopropane Both blood and plasma volumes are reduced, a hemoconcentration invariably occurs, indicating the loss is due to a decrease in plasma volume This hemoconcentration is due in part to the splenic constriction caused by ether, thus releasing additional erythrocytes into the systemic circulation Bleeding time, clotting time, and prothrombin time are not affected by ether

## Metabolic Effects

Ether disturbs metabolic processes more than the gases do Carbohydrate metabolism particularly is affected Blood sugar rises, often as much as 100 per cent due to glycogenolysis Presumably this results from sympathetic stimulation, the release of epinephrine, the liberation of sympathin, or possibly a combination of all three factors Reconversion of lactic acid to glucose is inhibited Lactic, phosphoric, and other fixed acids increase in the blood causing a decrease in serum bicarbonates and carbon dioxide combining

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be given with a minimum of equipment The objectionable features to ether are the difficult, prolonged induction, flammability, excessive secretions, the somnolence after long operations, the disturbances of metabolism, and the post anesthetic nausea and vomiting A fire hazard exists with ether alone or when it is combined with any of the gases Cauteries and other devices which may be sources of ignition must not be used


## REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 32

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 56

BEECHER H K ADAMS R Ether anesthesia in the presence of pulmonary tuberculosis *J A M A* 118 1204 1942

BISHOP H F CILBERTI B J and BAPENTRICK E H Venous pressure during surgical anesthesia *Anesthesiology* 13 297–301 1952

BLALOCK A Cardiac output during ether anesthesia *Arch Surg* 14 732 1927

CRAWFORD E J GALDINO M Changes in extra fluid volume renal function and electrolyte excretion by intravenous saline solution in short periods of anesthesia *Anesthesiology* 13 374–388 1952

ETSTEN B E Respiratory acidosis during intra thoracic surgery *J Thoracic Surg* 25 286 1953

HAGGARD H W The absorption distribution and elimination of ethyl ether *J Biol Chem* 59 737–795 1924

HERSHEY S G ZWEIFACH B W and ROVENSTINE E A The effects of depths of anesthesia on behavior of the peripheral vascular bed *Anesthesiology* 14 245–256 1953

KURTZ BENNETT and SHAPIRO Electrocardiographic changes during anesthesia *J A M A* 106 434 1936

LEIGH M D Acidosis during clinical anesthesia *Anesthesiology* 3 429–431 1942

McALLISTER F F and ROOT W S The neurogenic control of the circulation of dogs under ether anesthesia *Anesthesiology* 3 491–506 1942

MEEK W J HATHAWAY H R and ORTH O S The effects of ether chloroform and cyclopropane on cardiac automaticity *J Pharmacol & Exper Therap* 61 240 1937

PAPPER E M Renal function during general anesthesia in operation *J A M A* 152 1686 1953

SEEVERS M H *et al* The role of hypercapnia and pyrexia in production of ether convulsion *J Pharmacol & Exper Therap* 63 33 1938

STEWART H B The volatile anesthetics *Anesthesiology* 2 635 1941

STUTZMAN J W ALLEN C R and MEEK W J The prevention of cyclopropane epinephrine tachycardia by di ethyl ether *Anesthesiology* 3 259 1942


## VINYL ETHER

### Properties

Following the introduction and acceptance of ethylene as an anesthetic a number of unsaturated ethers were investigated in order to find a volatile drug which might be superior to ethyl ether From the structural formula it was presumed vinyl ether should possess both the advantages of ethylene and ether and possibly be devoid of the disadvantages of each Vinyl ether is the unsaturated counterpart of ethyl ether The compound is often referred

to as a hybrid of ether and ethylene, since it is chemically similar to both. Divinyl ether is a clear colorless liquid, whose vapors are not irritating and possess an ethereal odor. Divinyl ether boils close to room temperature (28 C.) and therefore volatilizes easily. Unsaturated ethers are not as stable as saturated ethers. Vinyl ether polymerizes to a gelatinous resin when allowed to stand for a period of several months, unless a stabilizer is added. Acids, heat, and light hasten the deterioration. An alkaline, organic stabilizer (alpha phenylnaphthylamine) insures a pure product for a minimum of two years after the date of manufacture. The contents remain stable for three or four days, once the package is opened. "Vinethene" is a proprietary name for a mixture of vinyl ether, 3.5 per cent alcohol and the amino chemical stabilizer (.05 per cent). The alcohol is added to raise the boiling point and to prevent the exhaled water vapor from freezing on the mask in the "open-drop" technique.

## Potency

The alveolar concentration for surgical anesthesia is 4 per cent, for respiratory failure, 8 per cent. The drug possesses a wide margin of safety. As in the case of ethyl ether, respiratory failure precedes circulatory failure. When respiratory failure occurs, the chances for successful resuscitation are good but not as good as for ethyl ether. Satisfactory analgesia is obtained with concentrations of 1 per cent or less.

Induction, like that of the gases, is brief, pleasant, and without struggling or excitement. The water and tissue solubility is like that of the gases. *Recovery is rapid without any delirium or excitement.* The drug is inert and is eliminated unchanged by exhalation within three or four minutes. The immediate post anesthetic period is free from nausea, vomiting, prolonged drowsiness, ataxia, and residual narcotic effects—notable features when anesthesia is desired for minor surgery in ambulatory patients. During induction stimulation of the salivary and mucous glands often causes troublesome secretions, particularly when anticholinergic drugs have been omitted.

## Effects on Respiration

The vapors of vinyl ether are neither pungent nor "irritating" when inhaled. The mouth of the container may be placed against the nostril and a deep inspiration may be taken without any disagreeable sensation. Violent coughing ensues when a similar attempt is made using ethyl ether. No induction agent, therefore, is necessary as in the case of ether. Indeed vinyl ether is widely used as the primary drug to facilitate induction of "open drop" ether.

Pharmacologically, vinyl ether may be considered "intermediate" between the gases and ethyl ether. The "stimulating" effects upon respiration are less pronounced than those of ethyl ether. Respiratory minute volume exchange

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is increased, but not to the extent it is with ethyl ether Vinyl ether is a bronchodilator

## Effects on Circulation

Myocardial depression and arrhythmias are infrequent Blood pressure, venous pressure, and pulse rate remain unaltered Sensitization of the conducting tissues to epinephrine does not occur

## Metabolic Effects

Blood chemical changes, likewise, are clinically insignificant Some disagreement exists concerning the effects of vinyl ether upon liver and kidney function In dogs anesthesia complicated by anoxia is followed by cloudy swelling, central necrosis, and other histologic changes of the liver parenchyma In addition, impairment of hepatic and renal function after repeated administrations, has been demonstrated in dogs Blood sugar, acid base balance, and blood nitrogen are not altered

## Effects on Smooth Muscle

Smooth muscle is progressively depressed as anesthesia deepens Intestinal motility and tone are depressed in the deeper planes of anesthesia Uterine activity is not depressed in light anesthesia, but it is in deep anesthesia The drug, therefore, is suitable as an anesthetic, and as an analgesic in the terminal stages of labor

## Convulsions Due to Ethers

Dogs anesthetized with vinyl ether manifest so called running movements These appear even though consciousness is absent and superficial reflexes are obtunded Such neuro muscular phenomena are due to stimulation of the sub cortical and spinal motor centers by the vinyl ether Occasionally, generalized convulsions occur during vinyl ether anesthesia in man They, too, are believed to have the same etiology Preliminary medication, using morphine, barbiturates, and other non volatile central nervous depressants, prevents their appearance or minimizes their severity The convulsions are common when vinyl ether is administered with nitrous oxide

The convulsions differ both in etiology and behavior from "ether convulsions," which appear during anesthesia with ethyl ether They are less serious and the prognosis is excellent Convulsions due to vinyl ether appear shortly after the administration of the drug is commenced They do not persist if the drug is discontinued immediately They are more frequent when anesthesia is deep They appear in the presence of adequate oxygenation and are not related to anoxia Ether convulsions, on the other hand, appear when anesthesia is well established, rarely before 15 or 20 minutes have elapsed They are aggravated by deepening anesthesia Infants, children, and youthful adults seem to be more susceptible Sepsis, fever, meta

bolic acidosis, dehydration, and disturbances of electrolyte balance are invariably present They are associated with hypoventilation, with the administration of carbon dioxide oxygen mixtures, and with rebreathing of carbon dioxide, in short, anything which predisposes to carbon dioxide retention Ether convulsions are accompanied by hyperthermia Whether it is the cause or the result of the convulsions is not known Convulsions occur more frequently in patients who have fever It is not uncommon for temperatures to rise above 106°F When the triad of anesthesia, respiratory acidosis, and metabolic acidosis are superimposed upon a septic state in a youthful subject with pyrexia, the stage is set for convulsions Convulsions due to vinyl ether are treated by merely discontinuing the anesthetic "Ether convulsions" are controlled with intravenous barbiturates Any device which permits rebreathing or carbon dioxide retention is to be discarded Further measures in therapy include efforts to reduce the body temperature, readjustment of the acid base balance, and correction of disturbances in electrolyte balance Differentiation must be made between convulsions due to anoxia to stimulating drugs, or to neurological lesions

## Clinical Uses of Vinyl Ether

Vinyl ether is used to facilitate induction of ethyl ether anesthesia by the "open drop" technique Minor surgical procedures requiring a few minutes anesthesia, such as myringotomy, incision and drainage of abscesses, removal of dressings and the like, may be performed with vinyl ether anesthesia Vinyl ether is used to fortify nitrous oxide or ethylene, when used by the semi closed method for dental or other surgery of similar magnitude Vinyl ether is flammable when mixed with air, oxygen, and nitrous oxide The usual precautions must be exercised to prevent fires and explosions

### REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 36

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 91

MARTIN S J ROVENSTINE E A. Vinethene A laboratory and clinical evaluation *Anesthesiology* 2 285 1941

ORTH O S SLOCUM H E STUTZMAN J W MEEK W J Studies of vinethene as an anesthetic agent *Anesthesiology* 1 246 1940

STEWART H B The volatile anesthetics *Anesthesiology* 2 635 1941

# CHLOROFORM

## Properties

Chloroform is a colorless, heavy liquid possessing a sweet, pungent odor The drug volatilizes with difficulty (B P 61°C ) at room temperature The vapor is approximately four times heavier than air, and is not flammable The compound easily oxidizes to phosgene in the presence of heat or light, or

when exposed to a flame or cautery Phosgene is converted to hydrochloric acid and carbon dioxide when it comes into contact with moisture in the alveoli Appreciable amounts cause pulmonary edema The alcohol which is added as a preservative combines with phosgene to form the relatively harmless ethyl carbonate

## Potency

Inhaled concentrations of chloroform which yield surgical anesthesia are approximately 1½ per cent 2 per cent concentrations cause respiratory failure *A narrow margin exists between the therapeutic dose and the lethal dose* More oxygen may be inhaled with chloroform than with any other anesthetic, 98 5 per cent, if one desires The vapor is not unpleasant to inhale at first, but becomes pungent and objectionable as anesthetic concentrations are approached Inasmuch as the induction is rapid and not unpleasant, chloroform may be used as a primary drug for induction preliminary to ether Recovery time varies After brief periods of anesthesia, recovery is rapid after long periods recovery is delayed Chloroform is a lipophilic anesthetic drug Its water solubility is poor compared to ether Desaturation is slow, however being more like that of ether than the gases Chloroform, like ether, is inert and undergoes no significant change in the body *It is eliminated almost entirely by the lungs*

Chloroform is the most potent inhalation anesthetic available Depth in all planes is obtained with ease Muscle relaxation is excellent

## Effects on Respiration

In many respects the pharmacologic effects of chloroform resemble those of ether The effects on the respiratory system are similar to, but less pronounced than those of ether Secretions are less copious or absent if the belladonna alkaloids are used As in the case of ether respiration is exaggerated but less so The causative mechanism is the same—effects of the drug on vagal nerve endings

## Circulatory Effects

The deleterious effects of chloroform on the cardiovascular system are well recognized During induction of anesthesia with chloroform vagal stimulation occurs Bradycardia and other irregularities appear Anticholinergic drugs administered prior to anesthesia prevent the response Chloroform sensitizes the automatic tissues to epinephrine and related amines in the same manner as cyclopropane does but to a lesser extent Ventricular tachycardia, ventricular nodal rhythm and even ventricular fibrillation may occur using the combination Spontaneous arrhythmias appear as anesthesia deepens As is the case with cyclopropane procaine or procaine amide intravenously prevent their appearance The chief objection to chloroform is

the depressant effect it exerts on the myocardium Cardiac output is reduced as anesthesia deepens Ultimately, asystole results Ordinarily respiratory failure, due to medullary paralysis, appears before asystole However, both may occur simultaneously or asystole may even precede respiratory failure

The blood concentration necessary for medullary depression also depresses the myocardium When overdosage occurs, the anesthetist is faced with two emergencies, respiratory failure, which must be overcome by artificial respiration, and circulatory failure, which can only be overcome by prompt cardiac massage Unless the thorax is opened immediately, efforts at cardiac resuscitation are usually fruitless Changes in the myocardium may be such that even massage is of no avail The most skillful and seasoned anesthetist is unable to foretell the eventual occurrence of circulatory collapse, because of the inherent cardiotoxic effect of the drug He may be powerless to overcome it, once it occurs The safety factor in chloroform anesthesia is beyond the skill and judgment of the anesthetist The use of chloroform as a surgical anesthetic is considered malpractice in certain areas of the United States

The vasomotor center is depressed during deep, prolonged chloroform anesthesia, contributing further to circulatory collapse Venous pressure rises as anesthesia deepens, due to the cardiac dilatation which accompanies myocardial depression Capillary permeability is increased more by chloroform than by any other inhalation anesthetic Blood and plasma volumes are decreased and a hemoconcentration occurs Chloroform constricts the normal spleen, causing release of erythrocytes into the circulatory stream

## Metabolic Effects

Blood chemical and metabolic changes differ little from those caused by ether but are more pronounced Acid base balance is disturbed, blood sugar rises, and liver glycogen is depleted as in the case of ether, but to a greater degree Liver function is disturbed Dye excretion may be impaired for several days depending upon the depth and duration of anesthesia and upon the degree of oxygenation Chloroform is the only inhalation anesthetic which significantly prolongs prothrombin time

## Effects on the Liver

Halogenated hydrocarbons are hepatotoxic, and chloroform is no exception The drug is used so little in the United States that statistical data concerning the incidence of hepatitis are not available Hepatitis which is characterized and followed by acute yellow atrophy, fever, jaundice, and manifestations of extreme hepatic insufficiency is a possible, and disastrous sequela of chloroform anesthesia The hepatitis appears several days after the administration of the anesthetic Pathologic findings are similar to those following carbon tetrachloride poisoning Central necrosis is the most common histologic change noted The possibility of hepatitis is enhanced by

starvation Preoperative feeding or intravenous administration of carbohydrates, amino acids, and intravenous xanthines decreases the incidence, as does administering the drug with oxygen

## Effects on Smooth Muscle

As in the case of ether, chloroform depresses smooth muscle in the gastro intestinal and genito urinary tracts Decreased motility and loss of tone occurs in the stomach, bowel, and uterus Labor is inhibited during light anesthesia, the uterus becomes atonic during deep anesthesia Practitioners in some areas of the United States favor chloroform for analgesia in obstetrics because its action is prompt, it is not disagreeable to the patient, and it is simple to administer When marked relaxation of the uterus for version or other operative obstetrics is desired, some obstetricians use chloroform The successful use of chloroform in obstetrics may be explained by the fact that it is used for analgesia and not for anesthesia More serious aspects of the chloroform problem would be encountered were the drug used for surgical anesthesia in the same manner as ether Chloroform is not flammable and is occasionally used for major surgical procedures when a fire hazard exists It may be used to fortify nitrous oxide The muscle relaxation obtained with chloroform is not equaled by any other inhalation anesthetic, except deep ether

### REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 40
ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 100
LUND R L Delayed chloroform poisoning in obstetric practice *Brit M J* *1* 489 1953
STEWART H B The volatile anesthetics. *Anesthesiology* *2* 635 1941
WATERS R M *Chloroform* Madison Univ Wisconsin Press 1952

# ETHYL CHLORIDE

## Description

Ethyl chloride (monochlorethane) at room temperature, is a gas which easily compresses to a colorless, highly volatile liquid (B P 12°C) The drug is dispensed in glass ampules equipped with a nozzle for dropping or spraying The vapor is heavier than air and flammable differing from chloroform in this latter respect Halogenation is not sufficient to render it non flammable The vapor is less objectionable than that of ether or chloroform, and it is inhaled without difficulty The alveolar concentration necessary for surgical anesthesia is 6 per cent The concentration which causes respiratory failure has not been established

Induction is rapid pleasant and without excitement, a feature which accounts for its sustained popularity Recovery, likewise, is rapid Within

three minutes, complete recovery occurs without nausea or the somnolence characteristic of ether or chloroform

## Systemic Effects

Ethyl chloride is similar to chloroform from a pharmacologic point of view Its cardiac effects are similar to chloroform Vagal stimulation occurs during induction Anti cholinergic drugs administered prior to anesthesia prevent it Spontaneous arrhythmias may occur during surgical anesthesia It enhances irritability of the automatic tissues Sensitization to epinephrine occurs as in the case of chloroform Ventricular fibrillation is a possibility when the drug is combined with epinephrine Myocardial depression occurs and cardiac output is decreased as anesthesia deepens Overdosage causes respiratory failure, but as in the case of chloroform, circulatory failure may precede respiratory failure Herein lies the chief objection to the drug as an inhalation anesthetic

## Effects on Respiration

The vapors are non irritating, easily inhaled and cause little or no secretions An increase in depth and rate of respiration occurs, as third stage anesthesia is established As in the case of chloroform and ether, the exaggeration of respiration is due to stimulation of the vagal nerve endings of the alveoli

## Metabolic Effects

The metabolic effects of ethyl chloride have not been studied in detail, because its use has been restricted to surgical procedures of a few minutes duration or for induction of "open drop" ether anesthesia It is assumed by most workers that they differ little from those of chloroform

## Uses

Ethyl chloride effectively abolishes superficial reflexes The "eye signs" are not wholly reliable The eyeballs continue to oscillate into deep third stage Ethyl chloride is not suitable for procedures necessitating muscle relaxation In fact, an increase in muscle tone occurs during light anesthesia and at times this gives rise to laryngeal spasm and to opisthotones Ordinarily ethyl chloride is administered by the "open drop" technique Its use as an inhalation anesthetic is not justified because of its cardiac effects The chances of resuscitation are poor in the event respiratory or circulatory failure occurs from overdosage

## Local Anesthetic Effects

Ethyl chloride may be used for local anesthesia The anesthetic effect is obtained by refrigeration of the tissues by allowing the liquid to evaporate as it is sprayed over the operative site The temperature under such circum

starvation Preoperative feeding or intravenous administration of carbo hydrates, amino acids, and intravenous xanthines decreases the incidence, as does administering the drug with oxygen

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REFERENCES

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ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 100

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and difficult. Anesthetic concentrations are pungent and not well tolerated. Analgesic concentrations are not objectionable to most patients. Salivation and excess mucous during anesthesia are troublesome. Both factors are responsible for the slow induction which characterizes inception of anesthesia with the drug. Effects upon respiration are similar to those of ether and chloroform. Instead of exaggerated breathing however, a tachypnea occurs. Sometimes the respiratory rate is 60 or more per minute. Presumably this results from vagal stimulation and indicates a dangerous state of physiologic disturbance.

Spontaneous arrhythmias occur during anesthesia, which indicate an increase in cardiac irritability. When trichlorethylene is used for analgesia, the arrhythmias are absent or occur less frequently. Evidence of a hepatoxic effect exists, particularly if the drug is not pure. Smooth muscle is relaxed in concentrations causing surgical anesthesia. Effects on smooth muscle in concentrations causing analgesia are not known. Analgesia does not interfere with the progress of labor.

Relaxation of skeletal muscle satisfactory for major surgery may be secured, but only after administration of the drug for a considerable period of time. There is little reason to use trichlorethylene for inhalation anesthesia. Its use as an analgesic is an entirely different matter, however.

The pharmacologic properties of trichlorethylene were investigated in both man and animals by Dennis Jackson and his associates in 1936. The Council on Pharmacy and Chemistry of the American Medical Association, after reviewing the data submitted, felt that its use as a general anesthetic was not justified.

## Toxicity

Prior to that study of the drug by Jackson, trichlorethylene was used for painful afflictions involving the area supplied by the fifth cranial nerve, on the basis that the drug was specific for that nerve. This contention has been disproved. It was dispensed in ampules similar to "pearls" used for amyl nitrite. Neuritis, palsies, areas of anesthesia, and other neurologic complications occasionally occur postoperatively. The cranial nerves, particularly the fifth, appear to be the most susceptible. These complications have occurred following its use as an inhalation anesthetic rather than after brief periods of analgesia. Recent evidence casts suspicion upon impurities in the drug, notably dichloracetylene, as the cause of these complications.

## Uses

Trichlorethylene is not recommended for surgical anesthesia. It is important to differentiate between analgesia and anesthesia. Great enthusiasm has been aroused concerning its analgesic effects. Several inhalers for self-administration by patients for analgesia during labor and other procedures

stances may be as low as —20°C Destruction of healthy tissue by freezing under such circumstances is common The anesthetic effect is not satisfactory as a rule Pain is often experienced as the frozen tissue is incised

REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 46
ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 96
BUSH O BITTENBENDER G ADRIANI J Electrocardiographic changes during ethyl chloride and vinyl ether anesthesia *Anesthesiology* 13 192 1952
HENDERSON V E KENNEDY A S Ethyl chloride *Canad M A J* 23 226–231 1930
KNOEFEL P K Pharmacology of ethyl chloride *Am J Surg* 19 282 1937
STEWART H B The volatile anesthetics *Anesthesiology* 2 635 1941

## TRICHLORETHYLENE

### Properties

Trichlorethylene or trilene, as the British have named it, has been used as a degreasing agent for dry cleaning purposes for many years It is a colorless, heavy liquid miscible with lipoids but poorly soluble in water It is an unsaturated halogenated hydrocarbon, being ethylene with three hydrogen atoms replaced by chlorine Its odor so closely resembles that of chloroform that it is colored with waxoline blue (in Great Britain) to avoid confusion Many of its physical properties resemble those of chloroform However it boils at a somewhat higher temperature (87°C )

Trichlorethylene is not entirely stable Oxidation converts it to phosgene Thymol is added as a stabilizer Contact with warm soda lime decomposes it to dichloracetylene The open or semi closed techniques are used for its administration the closed method utilizing alkaline substances for carbon dioxide cannot be employed Certain mixtures of trichlorethylene and pure oxygen are combustible but the concentrations used clinically are not flammable

### Potency

The concentration necessary for surgical anesthesia is approximately 4 per cent somewhat greater than that of chloroform The concentration necessary for respiratory failure in man has not been established Respiratory failure precedes circulatory failure when overdosage occurs Analgesia is obtained with concentrations of 1 per cent or less Most of the drug is eliminated unchanged through the lungs However some may be transformed to trichloracetic acid by the liver The trichloracetic acid is excreted into the urine

### Systemic Effects

The drug does not yield satisfactory anesthesia The induction period resembles that of ether more than that of the gases Vaporization is slow

## VI

# NON-VOLATILE DRUGS

### *Differences Between Volatile and Non Volatile Drugs*

Anesthetists no longer rely upon volatile drugs as the sole agents for anesthesia. Instead, combinations of inhalation anesthetics and non volatile drugs are used. Most non volatile drugs are not suitable, when used as the sole agents, for surgical anesthesia because they possess little or no analgesic potency. The pathways transmitting pain impulses from the periphery to the brain are not blocked completely by most of these substances. Reflexes are only partly obtunded, unless large doses are used. Supplemental analgesic drugs are required. The volatile drugs are inert in the body, the non volatile drugs are not. In many instances the non volatile drugs are detoxified entirely in the body, in others, they are eliminated partly by detoxification and partly by excretion, in an unchanged form, through the kidneys, sweat glands or gastro intestinal tract. The blood concentration may be no index of the amount present in the cells because they are often removed rapidly from the blood and stored in various tissues. Thiopental, for example, is stored in the lipoid tissues of the body from which it is gradually withdrawn and detoxified by the liver.

Non volatile drugs depress the nervous system from above downward. The degree of depression varies from a mild state known as *sedation* to a moderate state known as hypnosis, to a profound state known as basal narcosis, to a total state with loss of reflexes referred to as anesthesia. Doses which abolish reflexes and responses to painful stimuli completely inactivate the medullary centers and cause respiratory and circulatory depression (hypotension). There is a well defined distinction between hypnosis, basal narcosis, and narcosis. *Hypnosis* is a state of depression which causes sleep from which the subject may be aroused. There is no amnesia or disorientation. *Basal narcosis* is a more profound state of depression, from which the patient cannot be aroused or is aroused with difficulty. It is accompanied by amnesia. *Narcosis* is a general physiologic term implying depression of cellular activity without necessarily alluding to the central nervous system.

Depth of narcosis cannot be judged by Guedel's signs of anesthesia when a non volatile drug is administered as a sole agent or when one is administered in combination with volatile anesthetics. The orderly disappearance and reappearance of reflexes and other criteria of depth noted during the administration of volatile anesthetics is absent when non volatile drugs are employed. Certain non volatile drugs possess some analgesic properties. The narcotics such as morphine, meperidine, and similar drugs abolish percep

requiring analgesia have been introduced (Fig 12) Procedures such as removal of dressings, cystoscopic examinations and so on, formerly performed with no analgesia, may now be performed with trichlorethylene Trichlorethylene may be used in combination with nitrous oxide The comparative analgesic potency between this and other analgesic drugs remains to be established The test of time will determine its worth Any statement made at the present time would be premature



Fig 12 Inhaler for inducing analgesia with trichlorethylene The device may be held and used for self administration by the patient Air is drawn in through the bottom over a gauze wick and mixed with the vapors of the drug The mixture passes through a valve into the mask This valve closes during exhalation and a second valve which is set on top of the mask opens The vaporized drug and air enter the mask on inspiration The exhaled gases and vapors pass outside and are not rebreathed

## REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 44

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 76

WATERS R M ORTH O S and GILLESPIE N A Trichlorethylene anesthesia and cardiac rhythm *Anesthesiology* 4 1-5 1943

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tion to pain The sharp pain experienced during surgical procedures, however, is not abolished by narcotics the perception to dull pain is obtunded Narcotics, therefore, are not suitable as sole agents for surgical anesthesia

## Methods of Administration

Most non volatile drugs used for surgical anesthesia are administered intravenously or rectally No wholly satisfactory substances for basal narcosis are available for administration by the subcutaneous, intramuscular, or oral routes The majority of these substances are water soluble liquids possessing high boiling points, or they are solids In some instances, oils, such as polyethylene glycol or propylene glycol, are used as vehicles to prepare solutions for injection

## Chemistry of Non Volatile Drugs

Chemically the non volatile drugs are either aliphatic alcohols, aldehydes, ketones esters, sulphonmethanes, substituted amides, carbamates, ureides, and complex heterocyclic nitrogen containing substances Most of the heterocyclic nitrogen containing compounds are alkaloids The most useful alcohols are *ethyl alcohol, amylene hydrate,* and *pentynol* *Paraldehyde*, a polymer of acetaldehyde, does not possess a free aldehyde group *Tribromoethanol* and *trichlorethanol* are the most suitable halogenated alcohols *Chloral* is the most suitable halogenated aliphatic aldehyde The sulphonmethanes include *sulfonal, trional* and *tetronal* None of these are used in present day practice Although numerous substituted amides and ureas are available they are not widely used in present day practice The most important of the ureas are *bromural* and *carbromal* Various carbamates such as ethyl *urethane, hedonal* and *aponal* have had their day and passed into disuse The *barbiturates* are the most widely used non volatile hypnotics and basal narcotics They are ureides of the cyclic type The *narcotics* are non volatile substances, the majority of which are alkaloids or synthetic substances chemically similar to the alkaloids

Of all the non volatile drugs in current use the most important chemical types are the halogenated alcohols, the cyclic ureides (barbiturates), and the narcotics

## ETHYL ALCOHOL

It is not the scope of this book to discuss in detail the pharmacology of alcohol Ethyl alcohol has a limited value as a basal narcotic and as an anesthetic The margin between the therapeutic or anesthetic dose and the dose causing medullary depression is narrow Ethyl alcohol is occasionally used intravenously for analgesia and sedation

The blood level of ethyl alcohol commonly associated with intoxication is approximately 200 mgm or more per 100 cc A blood concentration of 50 to 100 mgm per cent suffices for sedation and analgesia when administered

by the intravenous route A sedative effect on the higher centers is obtained with this concentration This sedative effect is characterized by a dulling of the sensorium and the diminution of the power of concentration The euphoria and boisterousness which are usually indicative of the second stage of anesthesia, are absent The respiratory system and vascular system are not affected at this level Moderate vasodilatation occurs A solution composed of 5 per cent alcohol with 5 per cent dextrose in distilled water is used for intravenous administration No fixed dose can be established The rate of administration is adjusted to the clinical response of the patient An initial dose of 50 to 200 cc within the first 10 to 15 minutes causes an adequate response in most adults The intravenous drip is then adjusted to a rate of 3 to 8 cc (40 to 80 drops) per minute, the exact rate being determined by the response of the patient Intravenous alcohol has been suggested as a sedative for pre anesthetic medication for patients who are alcohol addicts for patients who have delirium tremens, and for patients who do not tolerate opium alkaloids for analgesia Intoxicated individuals are not difficult to anesthetize contrary to the erroneous impression of many physicians There is an additive effect between the alcohol and whatever other central nervous system depressant is used for analgesia

REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 52

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 108

## METHYL PENTYNOL

Methyl pentynol also known as methyl parafinol (Dormison) is a triple bonded unsaturated aliphatic alcohol This drug has been recently introduced as a hypnotic and sedative It is a liquid with a hydrocarbon like odor which boils at 200°C When administered orally in doses from 250–500 mgm it causes hypnosis It is rapidly absorbed from the gastrointestinal tract and excreted into the urine The alcohol is a mild hypnotic, somewhat more potent than amylene hydrate It is suitable for hypnosis for pre anesthetic medication Large doses cause respiratory depression and a fall in blood pressure The usual hypnotic doses are safe Repeated administration does not cause undesirable side effects Liver function renal function the concentration of blood constituents and so on are not altered during hypnosis The drug is dispensed in capsules containing 250 mgm or in the form of an elixir The onset of action after oral administration is manifested within 30 minutes and lasts several hours Patients may be aroused without disorientation or amnesia

REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 63

## AMYLENE HYDRATE

Amylene hydrate is known more for being the solvent for tribromoethanol than as a hypnotic and sedative Like other amyl alcohols, it possesses a mild hypnotic effect It is tertiary amyl alcohol In general, tertiary aliphatic alcohols are more potent than secondary alcohols, and the secondary ones more potent than primary Four cc of amylene hydrate intravenously induce a mild hypnotic state Amylene hydrate is not used as a hypnotic in present day practice Inasmuch as it is a solvent for tribromoethanol, its pharmacologic behavior is discussed under that heading

### REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 63

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 108

COUNCIL ON PHARMACY AND CHEMISTRY Avertin with amylene hydrate *J A M A* *109* 952 1937

## PARALDEHYDE

### Description

Paraldehyde is prepared by allowing acetaldehyde to polymerize in the presence of concentrated sulphuric acid Paraldehyde does not possess a free aldehyde group The substance is a clear, colorless, mobile liquid with a pungent odor, which appears to cling to the surrounding objects for days It is moderately soluble in water

### Uses

Paraldehyde has been used extensively for hypnosis and basal narcosis Orally 5 to 10 cc cause a dreamless hypnotic state which lasts several hours For deep hypnosis 15 to 30 cc in an equal volume of normal saline or olive oil are instilled rectally One cc of benzyl alcohol is added to alleviate local irritating effects Larger doses yield basal narcosis When administered intravenously, hynosis or basal narcosis results, depending upon the dose and rate of administration Responses are variable and the safety is not as great by the intravenous route

Paraldehyde is used very little in present day practice because its action is variable and it has a disagreeable odor and taste Frequently, the statement is made that paraldehyde is one of the safest hynotics The experiences of those who have used the drug consistently do not bear out this contention Its action is variable and the dose is difficult to estimate

### Systemic Effects

When used for basal narcosis, respiratory depression is common Overdosage results in respiratory failure Massive doses depress the myocardium Paraldehyde is not analgesic and restlessness follows its administration in the

presence of pain Large doses are required to obtund the superficial reflexes Such a state of narcosis is usually accompanied by respiratory depression Sedative doses do not have any notable effects on the vasomotor or respiratory centers The medulla is depressed in deep hypnosis, however The respiratory rate is increased during hypnosis and decreased in basal narcosis Ten to twenty per cent is exhaled *from the lung unchanged*, the remainder being detoxified by the liver The epithelium of the respiratory tract is "irritated" by the exhaled drug

During basal narcosis, oliguria occurs Diuresis follows in the recovery period Some of the drug is excreted unchanged into the urine, the concentration parallels the plasma *level*

During basal narcosis, the salivary and mucous glands pour out copious secretions unless an anti cholinergic drug is administered previously During basal narcosis smooth muscle is inhibited The drug passes through the placental membranes into the fetus causing depression of respiration at birth A cumulative action follows repeated use When administered intravenously, hemolysis, presumably due to its effect on the blood cells has been reported

### Disadvantages

Except in unusual circumstances paraldehyde is not recommended as a hypnotic, basal narcotic, or anesthetic The unpleasant odor, variability of action, lack of analgesic power, the narrow margin of safety in large doses, the irritating effect on the mucous membranes of the stomach, mouth, and rectum, and the metabolic disturbances that it induces during basal narcosis are the chief disadvantages

### REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed. Springfield Thomas 1953 p 55

ADRIANI J *The Chemistry of Anesthesia* Springfield Thomas 1946 p 145

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 175

KANE H F and ROTH Obstetrical Use of Paraldehyde *Anes and Analg* 19 282 1937

## TRIBROMOETHANOL (AVERTIN)

### *Properties*

Tribromoethanol or tribromethyl alcohol is a halogenated ethyl alcohol Three bromine atoms replace the hydrogen atoms opposite the hydroxyl bearing carbon of ethyl alcohol Halogenation of ethyl alcohol increases its narcotic potency considerably The substance is a white powder which is *poorly soluble in water* It forms a 3 per cent solution The compound is unstable when heated decomposing to various aldehydes and acids, most probably debromacetaldehyde and hydrobromic acid

Proctitis and colitis may follow the use of decomposed solutions Congo

red is added to solutions of avertin to detect the presence of acids which indicates that decomposition has occured Proctitis and colitis have also been reported following repeated administration over a period of several days Tribromoethanol melts at 80°C with decomposition The substance sublimes if allowed to stand in the open air In order to facilitate handling and storage it is dispensed as a solution in amylene hydrate One gram of the drug dissolved in one half gram of amylene hydrate, results in 1 cc of solution This solution is known by the proprietary name of *Avertin*

## Amylene Hydrate

The amylene hydrate possesses mild hypnotic properties, but in this case it merely serves as a vehicle for tribromoethanol The additive or potentiating effect of amylene hydrate which may occur with tribromoethanol is negligible

Amylene hydrate is a stable, colorless liquid which boils at 100°C In man, amylene hydrate is eliminated unchanged in the urine At body temperature, the vapor pressure is so low that the exhaled fraction is of no practical significance as far as the effects on lung parenchyma are concerned The general systemic effects of amylene hydrate are of no consequence when one considers the amount present in the volume of avertin fluid ordinarily employed

## Administration

Tribromoethanol may be administered intravenously but its action by this route is variable The response is at times fleeting, lasting a few minutes, only to be followed, after a latent interval, by severe depression When administered orally, it undergoes decomposition as it passes through the gastro intestinal tract The best results are obtained when it is administered by the rectal route A 3 per cent solution in distilled water, warmed to body temperature, is instilled into the rectum three quarters of an hour prior to the anticipated time of surgery A dose 30 to 40 mgm per pound of body weight is sufficient for adults Better results are obtained if the colon is cleansed with warm saline three or four hours prior to instillation The drug is rapidly absorbed from the entire colon When the ileocecal valve is patent, it passes into the small bowel from which absorption is even more rapid than in the large In the colon approximately 90 per cent is absorbed within the first 30 minutes Within 15 minutes, narcosis is established A peak effect occurs within 30 to 60 minutes followed by a gradual recession to the conscious state during the next hour The average duration of the basal narcosis is approximately two hours The patient, if undisturbed, remains well relaxed in a deep hypnotic state The superficial reflexes may be reactivated by painful stimuli The patient, however is aroused but is in a disoriented state Amnesia lasts approximately three hours Fatalities following the use of tribromoethanol are due to asphyxia from respiratory

obstruction or respiratory failure from overdosage Patients narcotized from tribromoethanol must not be left unattended The airway is maintained by supporting the chin and jaw Narcotized patients do not tolerate pharyngeal airways or endotracheal tubes Respiration, pulse, and blood pressure should be carefully followed

Surgery cannot be performed using tribromoethanol alone A supplemental anesthetic must also be used to supply analgesia Cyclopropane, nitrous oxide, ethylene, ether, vinyl ether, or trichlorethylene may be used Regional anesthesia properly performed may also be used as a supplement

## Detoxification

Tribromoethanol is conjugated with glycuronic acid by the liver A dose ordinarily employed for basal narcosis is detoxified within four hours when hepatic function is unimpaired Prolonged narcosis is not uncommon in the aged, and in chronically ill patients When liver or kidney functions are impaired, the elimination requires a longer period of time—sometimes days A cumulative action follows repeated administration

## Systemic Effects

Tribromoethanol depresses the medullary centers Respiratory depression is the rule rather than the exception Minute volume exchange is reduced 15 per cent Depression of the vasomotor center causes a transient hypotension in patients with a normal cardiovascular system The hypotension is more pronounced, of longer duration, and more serious in subjects with cardiovascular disease Unlike the halogenated hydrocarbons, basal narcotic doses of tribromoethanol have no effect on the heart Neither the cardiac output nor the conduction mechanism are adversely affected Any deleterious action on the circulation is secondary to the depression of the vasomotor and respiratory centers The pharyngeal, laryngeal, tracheal, and bronchial reflexes are only partly obtunded and are reactivated by mechanical stimulation or instrumentation

The drug is not suited for endoscopic work in the trachea, bronchi, and esophagus unless topical anesthesia is employed Motility and tone of smooth muscle are decreased The bronchi are dilated, gastro intestinal and uterine activity are inhibited The relaxing effect on the bronchi has been the basis for its use for intractable asthma The wisdom of using any drug which depresses respiration as much as tribromoethanol does, in the face of obstructive dyspnea is questioned The acid base balance is disturbed The hypoventilation causes a respiratory acidosis which is reflected in the general acid base balance pattern There is some reduction in carbon dioxide combining power and a slight lowering of serum pH In individuals whose electrolyte balance is not disturbed, this is of no special significance The drug is not suited for patients in acidosis or on the verge of acidosis Excre

tion of bromsulfalein is impaired The glycogen content of the liver is decreased, the output of bile salts is reduced Unlike chloroform and other halogenated hydrocarbons, hepatitis is uncommon following the administration of tribromoethanol As is the case with other hypnotics and basal narcotics, oliguria occurs during narcosis which is followed by a compensatory polyuria during recovery The non protein nitrogen and blood urea rise during narcosis, but return to normal afterward Plasma volume is reduced and some degree of hemoconcentration occurs The total blood carbon dioxide content rises slightly due to the depressed respiration

## Uses

Tribromoethanol is used as a basal narcotic for apprehensive, psychotic, disoriented, and uncooperative patients preliminary to surgery The basal narcosis it affords is useful for calming patients undergoing thyroidectomy for thyrotoxicosis, inasmuch as these are unusually apprehensive subjects Tribromoethanol has been widely used for neurosurgical procedures because it was believed that it lowered intracranial pressure This impression is not correct If a decrease in intracranial pressure occurs, it is the result of the hypotension which the drug may cause It certainly is not advised as the sole agent for neurosurgery, because it does not abolish painful impulses Furthermore, even when combined with local anesthesia, the operation invariably outlasts the period of narcosis, and some other form of anesthesia must be supplemented before the operation is completed Usually this is done to the disadvantage of the anesthetist and to the detriment of the patient There is no objection to its use, in conjunction with inhalation anesthesia endotracheally, for neurosurgical procedures

Tribromoethanol has been advocated as the sole agent also, for surgery of the eye because it decreases intra ocular tension Its disadvantages, administered in this manner for this type of surgery far outweigh any advantages gained by this supposed effect The same objectionable features are present for this type of surgery as in the case of neurosurgery Tribromoethanol is also useful to control the convulsive phase of tetanus, rabies, and toxic reactions to drugs Although popular fifteen or twenty years ago for basal narcosis, tribromoethanol has been supplanted by intravenous ultra short acting barbiturates These are simpler to administer and require no elaborate preparations, such as cleansing enemas, rectal installations and guessing the dosage

## Contraindications

Contraindications to the use of tribromoethanol are hepatic or renal disease, sepsis or "toxemia" from any cause, hypotension, acidosis, dehydration, reduced metabolic rate, pulmonary insufficiency of any type, and inflammatory diseases and neoplasms of the intestinal tract

REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 57

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 186

ADRIANI J *The Chemistry of Anesthesia* Springfield Thomas 1946 p 177

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 175

COUNCIL ON PHARMACY AND CHEMISTRY Avertin with Amylene Hydrate *J A M A* *109* 952 1937

## TRICHLORETHANOL

Trichlorethanol is similar to tribromoethanol It is a liquid which boils at 155°C with decomposition It is somewhat less potent and more variable in its action than tribromoethanol Larger doses may be necessary, but qualitatively, its responses are identical to those of tribromoethanol The uses, mode of administration, general pharmacological responses, detoxification, elimination, advantages, and disadvantages are similar to tribromoethanol The usual therapeutic dose is between 70 to 80 milligrams per pound of body weight Trichlorethanol is little used in present day practice Unlike tribromoethanol, trichlorethanol is not a propietory preparation It was originally introduced in an attempt to supplant tribromoethanol, which is patented and only available through a single manufacturer

REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 60

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield, Thomas 1947, p 186

ADRIANI J *The Chemistry of Anesthesia* Springfield Thomas 1946 p 177

## CHLORAL HYDRATE

Chloral is trichloracetaldehyde A hydrate forms by adding one molecule of water The former is a liquid, the latter a solid Chloral is derived from acetaldehyde Acetaldehyde possesses mild hypnotic properties, but it is irritating and is not clinically suitable Chlorination of the aldehyde markedly increases its narcotic potency and reduces its irritating effect The drug has a pungent odor and a sharp disagreeable taste Pharmacologically, chloral hydrate differs little from tribromoethanol Small doses cause a sedative and hypnotic effect Large doses cause basal narcosis It possesses no analgesic properties, and therefore must be combined with an analgesic when used for surgery Like trichlorethanol and tribromoethanol, its action intravenously is variable Although effective, if given orally, rectal administration is preferred for basal narcosis Like the halogenated alcohols, it is conjugated by the liver with glycuronic acid, and the urochloralic acid thus formed is excreted into the urine Medullary depression, hypoventilation, and hypo

tension occur when large doses are used, as is the case with tribromethanol when large doses are used Although useful as a sedative and hypnotic, chloral and chloral hydrate have little to offer over tribromoethanol as basal narcotics

## REFERENCES


ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas, 1953 p 62

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 175

VII

# NON-VOLATILE DRUGS (CONTINUED)

## BARBITURATES

### Chemistry and Derivation

Many hypnotic substances are derived from urea One group of derivatives of urea *in particular, the ureides, give rise to some of the most clinically useful hypnotics and basal narcotics* Ureides are formed when urea interacts with a carboxylic acid Ureides are either aliphatic or cyclic *Few of the aliphatic derivatives are of clinical value The cyclic ureides are important, however* Two types of cyclic ureides are recognized as clinically important, those derived from malonyl urea (barbiturates), and those derived *from glycocolic acid (hydantoins) Malonyl urea, also known as bar*biturie acid is made by condensing urea with malonic acid The hydantoins are made by condensing urea with glycocolic acid The former yields a six *membered ring the latter a five membered ring The hydantoins are cor*tical depressants The most important of these are *nirvanol* (ethyl phenyl hydantoin) and *dilantin* (diphenyl hydantoin) These are used to reduce *motor hyperactivity of cortical origin principally and are, therefore, of little* interest to anesthetists

### Potency of Barbiturates and Relationship to Chemical Structure

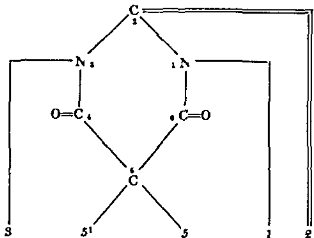
The barbiturates are widely used and are the most important hypnotics in clinical medicine Barbituric acid is not hypnotic Derivatives of barbituric acid *made by substituting alkyl, aromatic, and cyclic groups on the* carbon in position 5 yield sedatives and important hypnotics The ring in malonyl urea is identical to the pyrimidine ring which forms the bases cytosine, uracil and thymine which are found in nucleic acids When *malonic* acid is condensed with thiourea, thiobarbiturates form The thiouracil nucleus from which the anti thyroid drugs are derived possesses essentially the same nucleus as the thiobarbiturates

From a chemical standpoint four types of barbiturates are recognized (1) The ordinary *barbiturates* derived from barbituric acid, (2) the *N substituted barbiturates* in which an alkyl radical is substituted for one of the hydrogen atoms on one of the nitrogen atoms, (3) the *spirobarbiturates* in which the substituted radicals on position 5 are closed to form a ring, and (4) the *thiobarbiturates* in which a sulphur atom is placed, instead of the oxygen atom, on the urea residue in barbituric acid It is possible to

TABLE II

# PHARMACOLOGY OF BARBITURATES

Barbituric acid is a six membered ring possessing the pyrimidine nucleus The two hydrogen atoms on carbon 5 when substituted by aliphatic cyclic aromatic and other radicals yield numerous derivatives possessing hypnotic powers *The hydrogen atoms on either nitrogen atoms yield compounds called* N substituted barbiturates The oxygen atoms on carbon 4 and 6 remain intact Cyclic radical embodying carbon 5 results in spirobarbiturates




| Name | Fate | Action and Uses | 3 | 5[1] | 5 | 1 | 2 |
|---|---|---|---|---|---|---|---|
| Barbital (U S P) Medinal | Mostly unchanged eliminated five to seven days in urine | Long acting sedative | H | Ethyl | Ethyl | Na | O |
| Phenobarbital (U S P) Luminal (proprietary) | Eliminated unchanged recovered in urine | Long acting sedative | H | Phenyl | Ethyl | Na | O |
| Ipral (proprietary) | Partly destroyed and partly recovered in urine | Intermediate sedative | H | Ethyl | Isopropyl | Na Ca | O |
| Neonal (proprietary) | Partly destroyed and partly recovered in urine | Intermediate sedative | H | Ethyl | n Butyl | H | O |
| Dial (proprietary) | Mostly destroyed some in urine | Intermediate sedative | H | Allyl | Allyl | H | O |
| Alurate (proprietary) | Small part in urine mostly destroyed | Intermediate hypnotic | H | Allyl | Isopropyl | Na | O |
| Sandoptal (proprietary) | Destroyed none in urine | Short acting hypnotic | H | Allyl | Isobutyl | H | O |

TABLE II (continued)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Ortal (proprietary) | Destroyed none in urine | Short acting hypnotic | H | Ethyl | n Hexyl | Na | O |
| Amytal (proprietary) | Destroyed less than 3% in urine | Short acting hypnotic | H | Ethyl | Isoamyl | Na | O |
| Pentobarbital (U S P) Nembutal (proprietary) | Destroyed none in urine | Short acting hypnotic | H | Ethyl | 1 Methyl butyl | Na | O |
| Phanodorn (proprietary) | Destroyed less than 3% in urine | Short acting hypnotic | H | Ethyl | Cyclo hexenyl | H | O |
| Pernoston (proprietary) | Destroyed none in urine | Short acting basal hypnotic | H | β brom allyl | Butyl | H | O |
| Nostal (proprietary) | Destroyed none in urine | Short acting hypnotic | H | β brom allyl | Isopropyl | H | O |
| Evipal Evipan Hexabarbitone | Destroyed none in urine | Ultra short acting basal hypnotic | $CH_3$ | Methyl | Cyclo hexenyl | Na | O |
| Pentothal (proprietary) Thiopentone Thiopental | Destroyed none in urine | Ultra short acting basal hypnotic | H | Ethyl | 1 Methyl butyl | Na | S |
| Seconal (proprietary) | Destroyed none in urine | Hypnotic | H | Allyl | 1 Methyl butyl | Na | O |
| Delvinal Vinobarbital (proprietary) | Destroyed none in urine | Hypnotic | H | Ethyl | 1 Methyl 1 Butenyl | Na | O |
| Mebaral (proprietary) | Destroyed | Hypnotic anti-convulsant | $CH_3$ | Ethyl | Phenyl | Na | O |
| Butisol (proprietary) | Partly destroyed | Sedative and mildly hypnotic | H | Ethyl | Sec butyl | Na | O |
| Surital (proprietary) | Destroyed none in urine | Basal hypnotic | H | Ethyl | Allyl | Na | S |
| Thioethamyl (proprietary) | Destroyed none in urine | Basal hypnotic | H | Ethyl | Isoamyl | Na | S |
| Kemithal (proprietary) | Destroyed none in urine | Basal hypnotic | H | Allyl | Cyclo hexanyl | Na | S |

synthetize over a thousand barbiturates of various types Several hundred have been prepared, but of these only several dozen are in current use

## Pharmacological Grouping of Barbiturates

From a pharmacological standpoint, barbiturates may be placed into four groups *the long acting, the intermediate acting, the short acting,* and *the ultra short acting* Barbiturates as a class have certain features in common

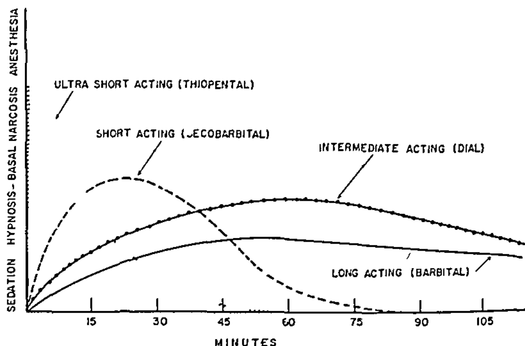



Fig 13 Curve showing the relationship of intensity or depth of depression and time using the various types of barbiturates The effect depicted is one obtained by using comparable doses intravenously Each type has a latent period and a point of maximum intensity or peak effect Note the latent period is shortest with the ultra short acting barbiturates is longer with the short and still longer with the intermediate and long acting types The peak effect is manifest soonest and is most intense with the ultra short acting barbiturates comes on later and less intense with the short and later still and less intense with the intermediate and long acting respectively

They cause sedation or cortical depression in small doses, hypnosis in larger doses, deep hypnosis or basal narcosis with still larger doses and anesthesia with complete abolition of reflexes with massive doses Basal narcosis is often accompanied by respiratory and circulatory depression and is followed by prolonged somnolence All barbiturates manifest a latent period extending from the moment of injection until the peak effect is attained (Fig 13) The latent period is longest with long acting barbiturates, and shortest with the ultra short acting Potency, duration of action, and pharmacologic grouping depend upon the chemical configuration of the molecule In order to use barbiturates judiciously, it is necessary to be familiar with their chemistry Familiarity with the chemo morphology of barbiturates makes

it possible to predict the potency and pharmacologic properties of an unknown compound by glancing at its structural formula. Substitution of two methyl groups in position 5 of malonyl urea results in a (low potency) sedative. When two ethyl groups are substituted, *barbital* is formed. Barbital is a mild sedative. It was the first clinically useful barbiturate (introduced in 1905 by Fischer and Dilthey). Increasing the number of carbon atoms in each alkyl group increases potency and shortens the latent period. Barbiturates possess a wide margin of safety. Potency and toxicity increase as the molecular weight increases. Both potency and toxicity parallel each other. When the total number of carbon atoms in both substituents exceeds eight (M.W. 250) the toxicity increases in a greater degree than potency. Potency and toxicity no longer parallel each other and the margin of safety is narrowed. Substitution of bromine for hydrogen on either radical increases potency. Substitution of alkyl radicals derived from primary alcohols yield compounds of lesser potency than radicals derived from secondary alcohols. Iso-amyl-ethyl barbituric acid (amybarbital) is less potent than methylbutylethyl barbituric acid (pentobarbital). The radicals in the former are derived from a primary alcohol, the latter from a secondary. Thiobarbiturates are more potent and rapid acting than the "ordinary" types. Branching in the side chain, unsaturation in the side chain and cyclic and aromatic substitutions result in more potent derivatives (Table II).

## THIOBARBITURATES

### Chemistry

Thio-barbiturates are of exceptional importance because they are widely used in clinical anesthesia. The prefix 'thio' indicates that a structure contains a sulphur atom. Thio derivatives are available which are counterparts of the 'ordinary' barbiturates. Thus pentobarbital with the oxygen atom on the urea residue replaced by a sulphur atom gives *thiopentobarbital* (thiopental). Secobarbital (seconal) gives rise to *thiosecobarbital* (surital). Amybarbital (amytal) gives rise to *thioethamyl*. These thiobarbiturates are more potent and shorter acting than their oxygen counterparts. Another thiobarbiturate which is little used in the United States but used more extensively in Great Britain is Kemithal. Although thiopental is the most widely used ultra short acting barbiturate and is regarded as a drug all unto itself, it must be remembered that it is merely one in the group of many barbiturates. It possesses nothing which merits its being placed apart from the others from a pharmacologic viewpoint, except that it is extensively used.

### Chemical and Physical Properties of Barbiturates

Barbiturates are weak acids which form salts. Barbiturates exhibit the

phenomenon known as keto enol isomerism The OH radical which results is capable of dissociating into the barbiturate radical and hydrogen ion Salts form by replacement of this hydrogen by sodium or some other metallic ion Sodium salts form alkaline solutions having a pH ranging between 9 and 10 Calcium salts are known also These are used for preparing tablets because they are not hygroscopic Salts are more soluble in water than the acid form The acid form is less soluble in water, but more soluble in most organic solvents Therefore salts are more suitable for parenteral administration Intramuscular and subcutaneous injection of some barbiturate solutions may cause slough, because they precipitate in tissues This is due to the alkalinity of the drugs Thrombosis is not uncommon after intravenous administration of concentrated solutions Inadvertent intra arterial injection causes spasm of the artery with subsequent development of gangrene in the part supplied by the vessel Most barbiturates are white powders The thiobarbiturates possess a yellowish tint and a peculiar sulphurous odor

## Stability

Aqueous solutions of barbiturates are not stable They readily decompose when allowed to stand in air or when sterilized by heat Consequently, the sterile powder is dispensed for parenteral administration The powder is dissolved in sterile distilled water or normal saline immediately before use This policy is applied particularly to ultra short acting barbiturates Some of the short acting and long acting barbiturates are dispensed in specially prepared solutions in sealed ampules for parenteral use A preparation of secobarbital dissolved in polyethylene glycol (MW 300) which is relatively non irritating to tissues and stable is available for intravenous and intramuscular use

## Uses of Barbiturates

The long acting barbiturates are prescribed when mild depression of the central nervous system over a long period of time is desired This type of barbiturate is particularly useful for sedation, for apprehension, and for psychic disturbances The intermediate acting barbiturates are useful for "heavier" sedation or for the insomnia of early morning hours Sleep is induced with a combination of an intermediate and a short acting barbiturate The short acting barbiturate acts first and the intermediate acts later and sustains the effect The short acting barbiturates are indicated for hypnosis, for sleeplessness, and for pre anesthetic medication The ultra short acting barbiturates have been used intravenously for surgical anesthesia, because of the rapidly obtained intense effect In present day practice they are widely used in combination with volatile anesthetics

## Mode of Action of Barbiturates

The manner in which these four types of barbiturates behave is due to

a number of factors (1) Their mode of elimination The ultra short acting barbiturates are detoxified by the liver The long acting are eliminated unchanged by the kidney Duration of action is closely allied to rate of elimination and hepatic disfunction (2) A renal threshold exists for barbiturates Therapeutic doses of long acting barbiturates are excreted almost entirely (over 90%) in the urine without change The intermediate acting barbiturates are partly detoxified and partly eliminated unchanged into the urine The short acting barbiturates do not appear in the urine except when massive doses are administered The ultra short acting barbiturates do not appear in the urine even when large doses are used Most long acting derivatives possess a low renal threshold They are stored in the tissues and slowly excreted A therapeutic dose of phenobarbital is normally excreted within 24 hours Short acting drugs possess a higher renal threshold, and for this reason they do not pass into the urine unless administered in large doses In over dosage or following the ingestion of large amounts for suicidal intent, short acting barbiturates such as secobarbital or pentobarbital may be recovered in the urine If large doses of long acting barbiturates are administered, the percentage of the total which appears in the urine unchanged is decreased even though the absolute quantity is increased This indicates that the long acting drugs may be detoxified in part by the liver when large amounts are ingested

## Analgesic Properties

Barbiturates possess little or no analgesic action Administration in the presence of pain may cause restlessness, disorientation, and excitement particularly if larger than usual doses are employed A progressive depression of the cerebrospinal axis occurs from above downward The initial sites of action are the cerebral cortex and sub cortical structures Response to pain may be abolished by doses which are considered unsafe Doses which depress the cortex do not necessarily abolish superficial reflexes The pain pathways from the periphery to the cortex remain intact External stimuli pass to the thalamus and thence to the cortex The short and ultra short acting derivatives, because of their greater potency, have a more pronounced effect than the long acting derivatives Doses necessary to abolish reflexes and responses to painful stimuli depress the medullary centers Respiratory and circulatory depression invariably occur Analgesic drugs must be combined with barbiturates when administered in the presence of pain to avert this difficulty Originally thiopental, evipal, and other ultra short acting barbiturates were used as the sole agents for anesthesia The total dose necessary to complete long operations is far in excess of the dose considered safe In present day practice ultra short acting barbiturates are used only for basal narcosis Combinations with nitrous oxide, ethylene, cyclopropane, trichlorethylene, and other anesthetic and analgesic substances must be used for

surgery Nitrous oxide and thiopental is the most widely used combination The efficiency of the volatile drug is increased and the amount of barbiturate necessary is reduced to a minimum Combinations may be used over longer periods of time before respiratory and circulatory depression develops

When used for hypnosis in painful conditions, barbiturates must be combined with analgesics such as demerol, codeine, acetylsalicylic acid, and so on to avoid disorientation

## Onset of Action

The onset of action of a barbiturate varies with the route of administration The onset is slowest by the oral route, then the rectal, then the intramuscular, the intra peritoneal, and is most rapid by the intravenous route Absorption from the gastro intestinal tract is variable Onset and duration are influenced by such factors as motility of the stomach and intestine, the relationship to meals (orally), evacuation of the colon (rectally), to dosage and to type drug Ultra short acting barbiturates may undergo partial destruction when administered orally or rectally One gram of evipal administered orally merely causes hypnosis, while one fourth of this dose intravenously induces basal narcosis When given rectally, approximately three times the intravenous dose is required for basal narcosis Short and long acting barbiturates are more stable when used orally or rectally The oral dose approximates the intravenous

Irrespective of the route used, there is a latent period from the moment of administration until the peak effect appears The latent period is shortened in the following order for each route for a given drug oral, intramuscular, rectal, intraperitoneal, and intravenous The intensity or peak effect is greatest and of briefest duration when administration is by the intravenous route The latent period is briefest for ultra short acting derivatives and increases as follows short acting, intermediate acting, and long acting Basal narcosis with intravenous thiopental is established within 40 to 50 seconds, with secobarbital in two to five minutes, with pentobarbital in four to eight minutes with amobarbital in seven to 10 minutes and with phenobarbital 15 to 20 minutes Giving the drug intravenously does not radically alter its pharmacologic behavior The importance of the latent period cannot be emphasized too strongly Overdosage has resulted from rapid repeated administration of short acting and long acting barbiturates, because sufficient time was not allowed for the effects to appear before repeating the dose

## Signs of Barbiturate Narcosis

A progressive depression of the central nervous system is observed when barbiturates are slowly administered intravenously The phylogenetically newer portions of the cerebrospinal axis are affected first, giving rise to phenomena akin to planes and stages of narcosis observed in the case of

aliphatic general anesthetics In the first stage consciousness is clouded This is due to slight or moderate depression of the cortex In the second stage the cortex is completely depressed Hypersensitivity to external stimuli ap pears There is slight depression of the sub cortical structures, particularly the subthalamic and motor nuclei Motor activity and excitement are absent, but there is increased sensitivity to external stimuli which initiate exagger ated movements

The third stage is that of basal narcosis When the cortical and dience phalic structures (thalamus, hypo thalamus and basal ganglia) are depressed, sensitivity to external stimuli is decreased and the response to pain is diminished In stage four the medulla is depressed Respiratory depression and circulatory collapse follow, the muscles are relaxed Rapid administra tion of short and ultra short acting barbiturates causes a telescoping and non appearance of these signs These signs are absent after sizable quantities of barbiturates have been given These stages can in no way be likened to those described for volatile anesthetics There is no such thing as a plane or a stage of "pentothal anesthesia"

## Systemic Effects

Hypnotic and sedative doses of barbiturates cause little, if any, notable systemic effects The progressive depression of the various phylogenetical layers of the brain gives rise to various states of depression encroaching upon deep hypnosis, basal narcosis, and ultimately anesthesia During basal narcosis if the brain stem is depressed, blood pressure falls The decrease in blood pressure is due to the effect on the vasomotor center The fall in blood pressure occurs more frequently in subjects with hypertension Ultra short acting barbiturates have been used in diagnostic tests to attempt to determine the possible therapeutic value of contemplated sympathectomy Increases in pulse rate occur, most likely a manifestation of compensatory readjustments of the circulatory system Therapeutic doses have little or no significant effect on the myocardium or conducting mechanisms Spon taneous arrhythmias are uncommon in man Unlike cyclopropane, sensitiza tion of the conductive tissues to epinephrine and other sympathomimetic amines does not occur As a matter of fact, barbiturates may afford a protec tive action under these circumstances

Total blood and plasma volume are more often expanded than decreased, but this depends on the barbiturate and the depth of depression As a rule the spleen dilates Red blood cells are withdrawn from the circulation, the hemoglobin and hematocrit values are reduced Bleeding time, clotting time, and cellular morphology are not altered

The respiratory depression initiates undesirable effects if anoxia occurs These differ little from the general effects of anoxia (see nitrous oxide), anoxia also causes constriction of the spleen and hemoconcentration Inas

much as there is respiratory depression followed by hypoventilation during basal narcosis with the ultra short acting barbiturates, respiratory acidosis is invariably present

Gastro intestinal tone and uterine activity are depressed during basal narcosis In hypnosis, the depression of smooth muscle is negligible Barbiturates all pass through the placental barrier to the fetus Fetal respiration may be depressed unless the quantity used is limited

Barbiturates do not disturb liver functions to a degree of clinical significance If basal narcosis is accompanied by anoxia, serious derangements may occur Long acting barbiturates are not necessarily contraindicated when hepatic insufficiency is present because the liver does not detoxify them The short and ultra short acting barbiturates are best avoided, however, since this organ does detoxify them Long acting barbiturates are best omitted when renal insufficiency is present, because they are eliminated by the kidney

Like the other central nervous system depressants, barbiturates temporarily inhibit urinary output There is a transient and functional derangement which persists during the period of depression The cause is not completely understood but it is believed to be partly due to intrarenal vasoconstriction and increased tubular reabsorption A transient oliguria occurs, the severity of which depends upon the degree of depression A compensatory polyuria follows in the recovery phase

Barbiturates do not cause any pathologic change in kidney, liver, heart or any other tissue of the body

Barbiturates cause little loss of muscle tone Relaxation occurs when dangerously large doses are administered in attempts to secure anesthesia In present day practice barbiturates are combined with muscle relaxants such as curare, decamethonium, and succinyl choline to obtain relaxation

## Detoxification

The liver detoxifies barbiturates, almost exclusively Liver function is not altered A drug which is detoxified by the liver does not necessarily damage or impair function of the organ When hepatic insufficiency is present, detoxification is retarded resulting in sustained depression for many hours Detoxification is also retarded when metabolism is reduced below normal In shock inanition, hypothyroidism, sepsis, acidosis, and cachexia the effects of barbiturates are prolonged There are variations in response from one individual to the next Duration and intensity of action may vary from one time to the next in the same individual with the same dose depending upon the metabolic state at the time of administration

The exact fate of each barbiturate is not known Presumably a degradation with a disruption of the malonyl urea ring occurs because the barbiturate cannot be recovered as such in the urine By products however have been identified Thiopental is quickly withdrawn from the blood stream and

stored in the fat depots in the skin, omentum and around the kidney The barbiturate is then transported to the liver where it is detoxified It is first oxidized to a di carboxylic acid The carboxyl groups replace both radicals on the carbon in position 5 From then on dismemberment of the ring occurs Disruption of the ring also occurs when amytal and certain other barbiturates are detoxified Thiopental is not destroyed by the plasma or serum

## Tolerance and Addiction

Repeated administration of a barbiturate gives rise to *tolerance* Progressively larger doses must be used to obtain a desired effect *Habituation* or physic dependence also follows daily administration of a barbiturate over a long period of time Although *physical dependence* or *addiction* does not occur as frequently or as readily as it does after repeated use of a narcotic, it is observed occasionally after prolonged administration of barbiturates Cross tolerance to barbiturates is a well recognized phenomenon A patient acquiring tolerance to one barbiturate after repeated use will also be tolerant to another which might be substituted for it at a later time

A phenomenon known as *intolerance* also occurs Small doses which ordinarily have no effect on the average individual induce an overwhelming depression in susceptible persons Intolerance may explain the fatalities from administration of comparatively small doses of thiopental and other barbiturates intravenously

Fortunately intolerance is not common When administering barbiturates intravenously, it is advisable to use a fractional test dose before proceeding with the administration of the estimated therapeutic dose On rare occasions a patient may exhibit the phenomenon known as idiosyncrasy In such a case the usual anticipated response of central nervous system depression does not occur Instead, bronchial spasm, dyspnea, excitement, convulsions, and response not characteristic of the drug are encountered Manifestations of allergy are noted occasionally in some individuals but these are rare Skin rashes and other cutaneous lesions are infrequent but may occur following the use of barbiturates

## Spasmogenic Activity

Barbiturates do not obtund or abolish reflexes in the pharynx, trachea, and bronchi In many instances they may be rendered more active, particularly when ultra short and short acting barbiturates are used Severe laryngeal and bronchial spasm may result from the slightest amount of secretions or mucus raised from the lower respiratory tract Such spasms are frequent when barbiturates are used for patients who have suppurative disease of the lung Although characteristic of all barbiturates, this spasmogenic effect is most intense with thiobarbiturates Blood resulting from instrumentation with nasal, pharyngeal, and tracheal airways, laryngoscopes, bronchoscopes, and that which passes into the pharynx during oral and

nasal surgery often initiates severe laryngeal spasm In order of decreasing spasmogenic activity are first, the ultra short acting thiobarbiturates, short acting, intermediate acting, and lastly, the long acting barbiturates Theoretically, the spasmogenic response should be counteracted by anti cholinergic drugs (atropine, scopolamine) because it is presumed to be of vagal origin Clinical experience does not bear out this contention, however No drug is entirely satisfactory in averting or overcoming laryngeal and bronchial spasm once it occurs Topical anesthesia is advised if instrumentation in the upper respiratory passages is contemplated Whenever possible, stimuli to these structures is to be avoided

## Anti Convulsive Properties of Barbiturates

Barbiturates are excellent anti convulsants, particularly when convulsions are due to central nervous system stimulation from drugs The ultra short acting and short acting barbiturates are more effective than the longer acting ones in the acute episodes Phenobarbital, which possesses a selective preference for the motor cortex, is the most suitable for sustained convulsive states

Various neuro muscular phenomena are occasionally observed during and after narcosis from the ultra short acting barbiturates Convulsions are known to occur after the administration of evipal During basal narcosis with evipal, fibrillary twitchings are often noted There is no adequate explanation for their occurrence It may be that the cortex is depressed and that sub cortical centers are active and give rise to these neuromuscular phenomena At the conclusion of surgical anesthesia in which thiopental has been used as a basal narcotic for a long period, twitchings and convulsive movements may occur Whether or not this is the result of carbon dioxide accumulation and respiratory acidosis which occurs during thiopental narcosis is not known, but it is definitely presumed by some to be so

During basal narcosis with the barbiturates, particularly in the ultra short acting derivatives, a progressive loss of sensitivity of the respiratory center to carbon dioxide occurs The carotid body remains active When the respiratory center no longer responds to carbon dioxide stimulation, anoxia occurs and the carotid body takes over and sustains respiration Oxygen administered under these circumstances results in apnea Further accumulation of carbon dioxide follows the apnea, due to the removal of the anoxic stimulus This excess carbon dioxide may initiate these so called convulsive manifestations

## REFERENCES

Adams R C *Intravenous Anesthesia* New York Hoeber 1944

Adriani J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 65

Adriani, J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 173

Adriani J *The Chemistry of Anesthesia* Springfield Thomas 1946 p 223

Anderson B M  Essex H E  Analysis of blood for certain barbiturates in the variability of their concentration in the blood  *Anesthesiology* 4 113–123, 1943

Barrett R K  The analeptic effect of sodium succinate on barbiturate depression in man  *Anesth & Analg* 26 63 1947

Cahn J B  Nicholson D B *et al*  Placental transmission of a thiobarbiturate in parturient woman  *Obst & Gynec* 1 633 1953

Goodman L and Gilman A  *The Pharmacological Basis of Therapeutics*  New York Macmillan 1941 p 126

Mark L C  Papper E M *et al*  Quantative pharmacologic studies with pentothal  *New York State J Med* 49 1546 1949

Orth O S  Wangeman C P and Meek W J  The failure of various barbiturates to prevent cyclopropane epinephrine ventricular tachycardia in the dog  *Anesthesiology* 2 628–635 1941

Papper E M  Renal function during general anesthesia in operation  *J A M A* 152 1686 1953

Pickrell L L and Richards R K  Pentothal metrazole antagonism  *Am J Surg* 121 495 1945

Seldon T H  Lundy J S  Essex H G  The effect of certain general anesthetic agents on the small blood vessels in the ear of the rabbit  *Anesthesiology* 3 146–157 1942

Tatum A L  Atkinson A J and Collins K H  Acute cocaine poisoning its prophylaxis and treatment in laboratory animals  *Jour Pharmacol & Exper Therap* 26 325 1925

Tucci J H  Brazier Mary A  Miles H W  Finesinger J E  A study of pentothal sodium anesthesia and a critical investigation of the use of succinate as an antidote  *Anesthesiology* 10 25–39 1949

VIII

# NON-VOLATILE DRUGS (CONTINUED)

## THE NARCOTICS

Narcotics are non volatile drugs which possess both analgesic and hypnotic activity They act by raising the threshold of and altering the psychic response to pain The dull aching types of pain are relieved more effectively than the sharp lancinating types Unless large doses are used, reflex activity is not abolished to an extent which permits surgery The narcotics, therefore, are suitable for relieving pain preoperatively, postoperatively, after trauma and so on, but not for surgical anesthesia Many narcotics induce a psychic effect often termed, "a sense of well being" or euphoria and an air of indifference toward circumstances existing at the moment Such a state of mental tranquility is desirable preoperatively Barbiturates and other hypnotics do not as a rule induce this response and are therefore inferior to the narcotics for physic sedation

Until recent years all the useful narcotics were derived from opium The opium alkaloids may be placed into two groups, those derived from *iso quinoline* and those derived from *phenanthrene* The most important of the former group is *papaverine*, a non narcotic anti spasmodic The phenanthrene group includes the narcotics most important of which is morphine Alterations of the morphine molecule result in variations in potency (Table III) Methylation yields codeine, acetylation yields heroin, oxidation and hydrogenation dihydromorphinone (dilaudid) and so on

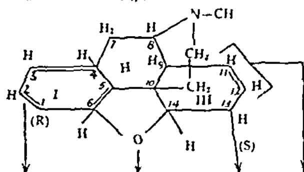
All these derivatives of morphine ultimately are derived from opium, inasmuch as morphine cannot be synthesized Synthetic substances are now available which possess both analgesic and hypnotic activity Their mode of action is qualitatively similar to narcotics derived from opium although quantitatively they differ Most important of these are meperidine (demerol), methadon dromoran (methyl morphinan) and nisentil None of these is derived from phenanthrene or is chemically related to morphine Their responses pharmacologically are similar to the opium alkaloids The similarities and differences are summarized in Table IV

When narcotics are administered repeatedly over a period of time, tolerance results The sense of well being leads to psychic dependence or habituation in susceptible individuals After several weeks of repeated administration, physical dependence or addiction develops In this state, it appears that the drug is necessary to maintain the necessary cellular functions Withdrawal results in symptoms and manifestation of organic disease, often called the

"abstinence syndrome" It is doubtful that several doses of a narcotic administered for some painful syndrome will cause addiction or start a strong willed individual on the path to addiction

TABLE III

The similarity and differences in the chemical structure of opium alkaloids and related synthetic substances derived from phenanthrene In general all have the same nucleus The column on the left shows the effect of altering the phenolic hydroxyl of morphine which is responsible for narcotic potency The ethereal oxygen remains unaltered in all compounds *The column on the right indicates the variations in the degree of unsaturation of ring III*




| | | | | |
|---|---|---|---|---|
| Morphine | HO— (Hydroxyl) | O | —OH (Hydroxyl) | H, H |
| Codeine (*Methyl morphine*) | $CH_3O$— (*Methoxy*) | O | —OH (*Methoxy*) | H, H |
| *Dionin* (Ethyl morphine) | $C_2H_5O$— (Ethoxy) | O | —OH (Hydroxyl) | H, H |
| Thebaine (Dimethyl morphine) | $CH_3O$— (Methoxy) | O | —$OCH_3$ (Methoxy) | H, H |
| Heroin (Diacetyl morphine) | $CH_3C(=O)-O-$ (Acetyl) | O | $-O-C(=O)-CH_3$ (*Acetyl*) | H, H |
| Dilaudid (Dihydro morphinone) | HO— (Hydroxyl) | O | =O (Ketonic) | —H, —$H_2$ |
| Dicodid (*Dihydromethyl morphinone*) | $CH_3O$— (*Methoxy*) | O | =O Ketonic | $H_2$, —$H_2$ |
| Metopon (Methyl dihydro morphinone) | OH (Hydroxyl) | O | =O Ketonic | —H—$CH_3$, $H_2$ |

TABLE IV

COMPARISON OF THE GENERAL PHARMACOLOGIC PROPERTIES OF MORPHINE AND THE VARIOUS SYNTHETIC NARCOTICS

| | Morphine | Meperidine | Methadon |
|---|---|---|---|
| Action on smooth muscle | Spasmogenic | Spasmolytic | Spasmogenic |
| Antitussive action | Suppresses cough | None | Like morphine |
| Action on respiratory center | Depresses | Depresses | Depresses |
| Parasympathetic effect | Stimulates | Atropine like action | Like morphine |
| Analgesic effect | Good | Between codeine and morphine | Like morphine |
| Hypnotic effect | Good | Less than morphine | Less than morphine |
| Addicting properties | Addicting | Less than morphine | Less than morphine |
| Action on pupil | Constricts | Dilates | Constricts |

## PREANESTHETIC MEDICATION

### Purpose of Premedication

*The type of preanesthetic medication selected depends upon the anesthetic procedure to be employed* Preanesthetic medication is a part of the anesthetic procedure As such, it should be prescribed and administered at a time determined by the anesthetist, since he knows the type of anesthetic which will be used, the technical problems involved and the possible difficulties which might be encountered during the procedure Preanesthetic medication is administered solely for the patient's safety and comfort Correct selection and timing facilitates the induction and maintenance of anesthesia Premedication accomplishes four purposes (1) It is necessary for psychic sedation to allay apprehension Psychic sedation is necessary if induction is to be uneventful When the patient is properly sedated, the second stage of anesthesia is quickly traversed Excitement and delerium and its attendant undesirable sequela are avoided (2) Premedication is used to obtain an additive effect between the anesthetic drug and the premedicating agent Anesthetics of mild potency such as nitrous oxide or ethylene are difficult to administer without decreasing the oxygen tension to less than physiologic levels When combined or fortified with other depressant drugs, *less gas is needed and more oxygen may be used* The margin of safety is thereby increased Drugs used for basal narcosis and the narcotics, morphine, dilaudid, meperidine or methadon, and so on reduce the metabolic rate and therefore reduce oxygen consumption This further adds to the margin of safety of nitrous oxide or ethylene Induction and maintenance of anesthesia using nitrous oxide or ethylene are thus facilitated

Emphasis has been placed by Guedel upon the importance of the reduction in metabolic rate by morphine In most cases, it is doubtful that the usefulness of premedication is due to its effect on metabolic rate (3) Premedication is necessary to minimize secretions in the upper respiratory tract During inhalation anesthesia, particularly when vapors of ethers and halogenated hydrocarbons are used, secretions in the upper respiratory passages cause obstruction to ventilation Anti cholinergic drugs are used to "dry up" secretions (4) Premedication is necessary for prophylactic reasons Anticipated untoward reactions occurring during anesthesia may be avoided by use of counteracting drugs Anticholinergic drugs, for example, may be administered in anticipation of laryngeal spasm during thiopental narcosis or cyclopropane anesthesia, and vagal reflexes with chloroform Barbiturates are administered prior to the use of sizable quantities of local anesthetics Stimulation and convulsions in the event of rapid absorption are partially counteracted Procaine amide, procaine, and quinidine are administered to avoid cardiac arrhythmias Barbiturates are frequently administered to avoid nausea in the postoperative period

## Type of Drugs Used

The selection of proper premedication depends upon the anesthetic drug selected, the method of administration, the age and physical status of the patient The narcotics are the most suitable and most frequently used drugs for sedation and for securing an additive effect Morphine, despite the numerous available substitutes, remains the drug of choice It possesses the hypnotic action necessary for psychic sedation and the analgesic action to combat pain in the event it is present The euphoria and sense of well being induced by narcotics instill in patients that sense of indifference and mental tranquility which is so essential for psychic sedation The dose of morphine is estimated in proportion to the metabolic rate As a rule the higher the metabolic rate, the larger the quantity of morphine per pound of body weight which is tolerated by the subject The lower the metabolic rate, the less the quantity of morphine which is tolerated

Some physicians, notably those who are not anesthetists, are opposed to the use of morphine for premedication They have no adequate basis for their dislike except that they do not "believe in or like morphine" Premedication, however, is not a doctrine to be accepted or rejected on the basis of belief or personal likes or dislikes Anyone well versed in the technique of administering inhalation anesthesia is familiar with the difficulties encountered when one administers inhalation anesthesia without a premedicating agent Omission of or inadequate premedication both makes the administration of anesthetics difficult and jeopardizes the patient Among anesthetists, Beecher has opposed the use of narcotics for premedication, but he stands almost alone in his belief

Dilaudid is as effective as morphine in proportionate doses Pantopon,

a purified aqueous extract of opium, contains approximately 15 mgm of morphine per 20 mgm of drug It is equally as satisfactory as morphine Codeine possesses insufficient hypnotic action to be suitable for adults Synthetic analgesics such as meperidine (demerol), methadon (levo isomethadon), and morphinan (dromoran) are effective analgesics They do not possess as much hypnotic activity as does morphine, and therefore are not as satisfactory for psychic sedation They may be combined with hypnotic drugs, for example, the short acting barbiturates They are used when the opium alkaloids are contraindicated Clinical experience has demonstrated that the barbiturates used alone for premedication are not as suitable as the narcotics One would expect them to be, on theoretical grounds, but clinical practice has demonstrated that they are inferior to narcotics Barbiturates, and other non volatile drugs, non narcotic drugs are effective when used in amounts which induce basal narcosis

The best and most popular combination for inhalation anesthesia is a mixture of morphine or other narcotic and scopolamine Scopolamine possesses a dual action—one on the central nervous system and one peripherally on the cholinergic postganglionic autonomic nerve fibers This latter action will be described later Centrally, scopolamine depresses the cortex and causes hypnosis Combined with morphine and other narcotics, it causes further cortical depression Sedation and amnesia lasting several hours are obtained using the combination The brain stem is not depressed, in fact, in most instances it is stimulated The respiratory depression caused by morphine is antagonized by scopolamine Atropine not only does not enhance the hypnotic and amnesic action of morphine, but even tends to antagonize it Waters suggests the effective ratio to be 25 parts of morphine to 1 of scopolamine (¼ gr morphine and $\frac{1}{100}$ gr scopolamine) The optimal effects are obtained when the drug is administered subcutaneously one to one and one half hours prior to anesthesia If administered too far in advance of the time of operation, the effects gradually recede and a supplementary dose is required The error of not allowing sufficient time to elapse before the effect of the drug can be established is unpardonable The purpose for which the premedication is prescribed is not fulfilled Over premedication creates a number of difficulties When inhalation anesthesia is used, the respiratory depression caused by overpremedication decreases ventilation which makes induction of anesthesia difficult When some form of regional anesthesia is selected such as spinal, or epidural or a nerve block, the sedation prevents the patient from complaining of pain during establishment of the block In emergency surgery where time is a factor, the combination of narcotic and anticholinergic drug may be administered intravenously, allowing three to four minutes for the injection Usually the effect is established within five to ten minutes When used intravenously, approximately two thirds of the dose should be used and supplemented further if necessary

## Variation in Dosage

Dosage is based upon the age and metabolic rate of the patient The response is more variable and less predictable at the extremes of age Children tolerate larger doses per pound of body weight than adults Patients in the older age groups have lower metabolic rates The dose is reduced in proportion Females, because of difference in size, usually require less than males *The metabolic rate is increased by fever approximately 7 per cent per* degree Fahrenheit Patients with fever theoretically should tolerate larger doses than those who are afebrile In actual practice this is not so, however Febrile patients are usually acutely ill from infectious diseases or other causes The response more often is one of greater depression than usual It is advisable, then, to use less than the usual dose in these cases and to supplement the dose with an additional amount later if more is indicated Patients who are in shock, who have acidosis, dyspnea due to diminished pulmonary reserve, respiratory obstruction of any sort, dehydration, or liver insufficiency should be given narcotics cautiously, if at all Narcotics are ordinarily omitted when increased intracranial pressure exists from any cause Although central nervous system depressants may not cause an appreciable increase in intracranial pressure in themselves they may cause this response by interfering with ventilation An increase in carbon dioxide tension or oxygen lack or both cause dilatation of the cerebral vessels which in turn causes an elevation in intracranial pressure Narcotics are omitted in obstetrics for the obvious reasons that they may interfere with labor and cause respiratory depression in the new born

## Basal Narcosis Prior to Anesthesia

The induction of basal narcosis prior to anesthesia with non volatile, non narcotic, central nervous system depressants is a common and invaluable practice, particularly when *patients are uncooperative or extremely apprehensive* The basal narcosis is usually induced in the patient's room Thiopental, thiosecobarbital, and evipal intravenously or rectally are suitable *and are extensively used For adults the intravenous route is preferred* The drug is discontinued when the operating room is readied and anesthesia is induced The rectal route is used for infants and children, because attempting intravenous injection in these subjects is difficult at times One gram of thiopental or thiosecobarbital or evipal per 50 pounds of body weight is the usual dose for rectal administration Secobarbital or pentobarbital intravenously (100 to 250 mg ) has the advantage over thiopental in that only a single injection is required Continous intravenous administration of the thiopental is thus obviated This is an advantage when the patient is being transported from the room to the surgical unit The hypnosis obtained when short acting drugs are used is not as intense as it is with thiopental, but it is longer lasting

Tribromoethanol rectally is satisfactory also, but it entails more elaborate preparations and has been supplanted by the intravenous thiobarbiturates Paraldehyde in oil or in saline administered rectally is used on occasions, but it is not desirable because of its disagreeable odor, irritating effects, and variability of action Ethyl alcohol intravenously has been recommended, but is used only in exceptional circumstances such as pre medicating a chronic alcoholic or narcotic addicts Contrary to popular belief, the acute alcoholic patient is not difficult to anesthetize because he is already pre medicated It is the un premedicated chronic alcoholic patient who is difficult The narcotic should be omitted when prescribing narcotics for addicts who are cured An addict who is not cured obviously requires larger doses of a narcotic than a non addict Usually the dose to which the addict has been accustomed is the one that is to be selected for premedication

## REFERENCES


ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed. Springfield Thomas 1953 pp 77–81 pp 119–122

ADRIANI J *The Techniques and Procedures of Anesthesia*. Springfield Thomas 1947 p 9

ADRIANI J *The Chemistry of Anesthesia* Springfield Thomas 1946 p 211

ALEXANDER, F D A. and CULLEN S C Premedication. *Am J Surg* *34* 428 1956

BEECHER, HENRY K. Pain and some factors that modify it. *Anesthesiology* *12* 633–641 1951

DRIPPS R. D and DUMKE, P R. The effect of narcotics on the balance between central and chemoreceptor control of respiration. *J Pharmacol & Exper Therap* *3* 290 1943

GOODMAN L. and GILMAN A. *The Pharmacological Basis of Therapeutics* New York, Macmillan 1941 p 186

GUEDEL A. E *Inhalation Anesthesia*. New York, Macmillan 1950

GUEDEL A. E. Metabolism and reflex irritability in anesthesia. *J.A.M.A* *83* 1736 1924

WATERS R M. BENNETT J H and LEIGH M D The effects upon human subjects of morphine and scopolamine alone and combined. *J Pharmacol & Exper Therap* *3* 290 1943

## IX

# ANTI-CHOLINERGIC DRUGS

### Nature of Belladonna Alkaloids

The most satisfactory drugs for inhibiting secretion of mucus and saliva in the mouth and upper respiratory tract are the belladonna alkaloids Three alkaloids are available atropine, hyoscyamine, and scopolamine (hyoscine) These are all related chemically, being esters of tropic acid All three possess both a central and a peripheral action Atropine stimulates all components of the cerebral spinal axis mildly, but equally The cortical stimulation tends to antagonize the sedative effects of morphine, and other narcotics, when the combination is used for premedication However, the effects on the me dulla are desirable because they tend to overcome the depressant action of the narcotics on the respiratory center Atropine and hyoscyamine are tropine tropate Tropine tropate is optically active Hyoscyamine is the levo isomer Atropine is the racemic derivative containing both the dextro and levo components Therefore, it is optically inactive As a general rule the levo derivatives are the ones which occur naturally As a rule they are more active, physiologically, than the racemic or the dextro compounds This appears to be the case with hyoscyamine It is more active and more potent than atro pine Scopolamine is levo scopine tropate Unlike atropine, scopolamine is optically active The racemic and the dextro forms are believed to cause side actions and are not used

### Action of Belladonna Alkaloids

Of the three alkaloids, atropine appears to have the least "drying" effect and the most side actions Flushing of the skin and tachycardia are common with atropine In children particularly, the anti secretory action of atropine during anesthesia appears variable and feeble Both scopolamine and hyo scyamine are superior The tachycardia and the flushing do not occur when scopolamine or hyoscyamine are used Many physicians who practice pedi atrics are opposed to the use of atropine in infants and children undergoing surgery on the supposition that it causes thermal reactions postoperatively Elevations in temperature are unusual when single doses of belladonna alka loids are administered for pre anesthetic medication to infants or children They do occur frequently from a cumulative action when the belladonna alkaloids are used in repeated doses for the relief of pyloric spasm and other clinical syndromes accompanied by vagal overactivity

In pediatric anesthesia, excessive secretions not only are vexsome to the anesthetist but jeopardize the patient Obstruction and hypoventilation

invariably occur if secretions are excessive Asphyxia is responsible for the majority of fatalities during general anesthesia on the operating table Obstruction due to excessive secretions accounts for a large proportion of these fatalities Mishaps from asphyxia during anesthesia are more frequent than fatalities from over dose of atropine As a matter of fact, authorities on pharmacology and toxicology agree that fatalities due to overdosage of atropine are rare Therefore, one has to choose between the possibility of death from asphyxia or a possible elevation in temperature from an untoward reaction to atropine The latter is much easier to combat than an obstructed airway during inhalation anesthesia There is no doubt in the minds of most anesthetists as to whether or not an anti cholinergic drug should or should not be used Anesthetists ' believe" in atropine

The newer anti-cholinergic drugs such as antrenyl and banthine possess some 'drying effect" as far as secretions are concerned They have little to offer over hyoscyamine, scopolamine, and atropine and certainly do not provide the sedative effect which is so desirable and characteristic of scopolamine In adults, therefore, they are of little value There is little justification for prescribing them In pediatric anesthesia banthine has caused hyperthermia, marked tachycardia, and other side actions Unless the drug is carefully used, side reactions are difficult to eliminate Its use for pediatric anesthesia is not advised

## REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1955 pp 100–105 pp. 119–121

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 460

GRIGGS T ADRIANI J and BERSON W Aids to Pediatric Anesthesia *Anesth & Analg* 32 340 1953

# X

# LOCAL ANESTHETICS

## CHEMISTRY OF LOCAL ANESTHETICS

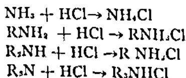
From a chemical standpoint, local anesthetics may be placed into two groups The first and most important group includes the majority of drugs in current use This group is composed of complex nitrogen containing compounds Their structures all conform to a general configuration Three groups and linkages are recognized in their molecules (1) An aromatic nucleus, (2) a nitrogen atom or nitrogen containing a heterocyclic nucleus, and (3) an intervening side chain which separates these two One or two atoms of nitrogen usually in the form of an amino group is always present in the molecule In some compounds, in procaine for example, an amino group is also found on both the aromatic nucleus and the terminal carbon of the side chain The amino groups, which are usually tertiary or secondary, confer basic properties of these derivatives

The second group of local anesthetics, one which is relatively unimportant, consists of hydroxy compounds These are aromatic, aliphatic, or hetero cyclic derivatives *Chloretone, phenol, benzyl alcohol, bromsalizol, saligenin,* and menthol are typical examples in this group They act by causing local irritation or nerve destruction rather than by causing a physiologic blockade They are used for surface anesthesia and rarely for infiltration Inasmuch as the nitrogen containing compounds are the most important they will be considered in detail

The majority of local anesthetics of importance are esters, that is they are composed of an organic acid and an alcohol The alcohol usually has the nitrogen atom Others are amides in which the intervening side chain replaces a hydrogen atom Others such as lidocaine are analides, that is they are analine or other aromatic amines with one hydrogen atom replaced by the intervening side chain to which is attached the nitrogen atom

### Chemical Properties

With the exception of cocaine, the currently used local anesthetic drugs are *synthetic* substances Since they are basic compounds, they react with acids *such* as hydrochloric, sulphuric, lactic, boracic, acetic and others to form salts The reaction is similar to the formation of a salt by *ammonia* and an acid



$$NH_3 + HCl \rightarrow NH_4Cl$$
$$RNH_2 + HCl \rightarrow RNH_3Cl$$
$$R_2NH + HCl \rightarrow R_2NH_2Cl$$
$$R_3N + HCl \rightarrow R_3NHCl$$

The salts for the most part are solid, crystalline substances soluble in water Aqueous solutions of salts are acid in reaction The addition of alkalis to solutions of salts causes precipitation of the free base The basic forms are usually high boiling point liquids or amorphous solids The bases are less soluble in water and less stable than the salts The bases readily dissolve in lipoids and lipoid solvents, a fact of importance in the preparation of ointments and oily solutions Salts do not dissolve as readily in lipoids and oils and are therefore not suitable in many instances for preparation of ointments Local anesthetics differ little from alkaloids in chemical nature and behavior They possess many chemical and physical properties characteristic of alkaloids They respond to the same color tests and precipitation reactions as do alkaloids when treated with alkaloidal reagents

### Para Amino Benzoic Acid Derivatives

Among the esters, the most important local anesthetics are derived from paramino benzoic acid When this acid is esterified with ethyl alcohol, ethyl paramino benzoate forms, with butyl alcohol, butyl paramino benzoate or *butesin* forms The ethyl paramino benzoate derivative is known as benzocaine (anesthesin) These substances are poorly soluble in water and possess a low toxicity and potency They are used exclusively in ointments for surface anesthesia Procaine (novocaine), the best known drug of this series, forms when paramino benzoic acid is esterified with di ethyl amino ethanol This compound is the same as benzocaine except that it has added to the terminal carbon of the alcohol, an amino group which has the two hydrogen atoms replaced by ethyl groups It is, therefore, an ester of para aminobenzoic acid and diethyl amino ethanol This modification results in a compound which is water soluble and is more potent and more toxic Tetracaine (pontocaine), monocaine, amylcaine, butyn, larocaine, and tutocaine are also esters of paraminobenzoic acid and some amino alcohol (Table V)

### Benzoic Acid Derivatives

Another important series of esters is derived from benzoic acid Cocaine and piperocaine (metycaine) are two currently used drugs in this series (Table VI) Cocaine is a benzoic acid ester of methyl ecgonine A number of less toxic compounds have been prepared from cocaine by modifying the ecgonine portion of the cocaine molecule The alpha and beta eucaines, the tropacocaines and piperocaine are notable examples of derivatives in this group Of these piperocaine is the only one which is currently employed Stovaine and alypin are benzoates of aliphatic amino alcohols

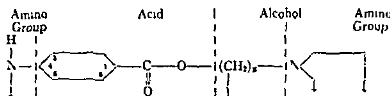
### Other Esters

Another group of esters is formed from cinnamic acid, the most important drug of which is apothesine Another series is formed by esterifying para

ethoxy benzoic acid with amino alcohols This acid merely replaces the amino group of amino benzoic acid with the para ethoxy ($O-C_2H_5$) group The homologue to procaine in this series has recently been marketed as *intracaine*

TABLE V

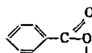
Local anesthetic drugs derived from aminobenzoic acid Drugs marked with an asterisk are derived from the ortho acid *The remainder from para aminobenzoic acid All are esters* Drugs above the dotted line are simple esters derived from alcohols containing *no nitrogen (insoluble group)*




| | | | | | |
|---|---|---|---|---|---|
| Benzocaine | H | | $-CH_2-CH_3$ Ethyl | No $NH_2$ | No $NH_2$ |
| Propaesin | H | | $-CH_2-CH_2-CH_3$ Propyl | No $NH_2$ | No $NH_2$ |
| Butesin | H | | $-CH_2-CH_2-CH_2-CH_3$ Butyl | No $NH_2$ | No $NH_2$ |
| Orthoform | OH | $NH_2$ on position 3 No $NH_2$ on 4 | $CH_3$ Methyl | No $NH_2$ | No NH |
| Orthoform (New) | OH | OH on position 3 | $CH_3$ *Methyl* | No $NH_2$ | No $NH_2$ |
| Procaine | H | | $-CH_2-CH_2-$ | $-C_2H_5$ | $-C_2H_5$ |
| Butyn | H | | $-CH_2-CH_2-CH_2-$ | $-C_4H_9$ | $-C_4H_9$ |
| Pontocaine | $C_4H_9$ | | $-CH_2-CH_2-$ | $-CH_3$ | $-CH_3$ |
| Larocaine | H | | $-CH-C(CH_3)(CH_3)-CH-$ | $-C_2H_5$ | $-C_2H_5$ |
| Tutocaine | H | | $-CH(CH_3)-CH(CH_3)-CH-$ (H) | $-CH_3$ | $-CH_3$ |
| Isocaine | H | | $-CH_2-CH_2-$ | $C_3H_7$ Iso | $C_3H_7$ Iso |
| Monocaine | H | | $-CH_2CH-$ | $C_4H_9$ (Iso) | H |
| Amylcaine | H | | $-CH_2CH_2-$ | $C_5H_{11}$ | H |

TABLL VI

I ocal anesthetic drugs which are esters of benzoic acid




| | |
|---|---|
| Stovaine | C(—$CH_3$)(—$C_2H_5$)—$CH_2$—N($CH_3$)($CH_3$) |
| Alypin | C(—$CH_2$—N($CH_3$)($CH_3$))(—$C_2H_5$)—$CH_2$—N($CH_3$)($CH_3$) |
| Metycaine | H—C(H)(H)—C(H)(H)—C(H)(H)—N ring: $H_2$C—C$H_2$, $CH_2$, C—$CH_2$, H, $CH_3$ |
| Eucaine (B) | ring: C—H, $H_2$C—C=$(CH_3)_2$, N—H, C(H)—CH—$CH_3$ |
| Cocaine | $H_2$C—C(H)—$CH_2$; →C—H, N—$CH_3$; $CH_3OOC$C(H)—C(H)—$CH_2$ |

NON ESTER TYPE DRUGS

In the non ester type drug *dibucaine* which is derived from quinoline is a substituted amide *Eucupine,* somewhat similar in structure to quinine, is a cupreine Lidocaine (xylocaine) is an analide type of compound Holocaine is prepared from para ethoxy aniline (phenetidin) which forms a basis of phenacetin and other anti pyretic drugs As in the case of the esters these compounds are basic and form salts

Overlapping of drug actions is common in pharmacology Many antihistaminic drugs manifest local anesthetic, anticholinergic and sedative effects The local anesthetic effects of most antihistaminics are of academic interest rather than clinical importance Anticholinergic drugs such as atropine, syntropan, and hyoscyamine possess a mild local anesthetic action Certain sympathomimetic amines (ephedrine) also have weak local anesthetic effects Mephanesin and certain steroid hormones are also local anesthetics As in the case of the antihistaminics, none of these is of clinical importance

## PHARMACOLOGY OF LOCAL ANESTHETICS

### Mode of Action

Local anesthetics, in contra distinction to general anesthetics, exert their effects at the site of application of the drug The mechanisms by which they cause a blockade are still topics of speculation Conduction of impulses through the segment affected by the drug ceases entirely The nerve fiber on either side of the narcotized area is active however The drug alters permeability of the cellular membrane which in turn disturbs the concentration of various ions, particularly potassium, in the surface layers of the cell The concentration of potassium in the surrounding medium is increased during the blockade The addition of potassium ion to solutions of local anesthetics potentiates the blockade Presumably the potassium ion alters the electrical polarity of the neural membrane and interferes with the transmission of the excitation wave It has been postulated that local anesthetic drugs cause an ultra microscopic coagulation of the colloids in the nerve cells which results in a reduction of activity The basic forms of local anesthetic drugs are lipophilic, that is, they are soluble in lipoids In this respect they are similar to general anesthetics An affinity exists between these drugs and cells of high lipoid content such as those of the nervous system

The usefulness of a local anesthetic drug depends upon three factors, its *solubility* its *potency*, and its *toxicity* Obviously, local anesthetic drugs must be water soluble to some degree to be carried into the cells Benzocaine, butesin, and propasin are relatively ineffective, because they are poorly soluble in water Numerous local anesthetics have been prepared whose usefulness is limited because of poor water solubility

### Potency

The potency of local anesthetic drugs depends upon the configuration of the molecules The chemical structure influences certain physical factors, particularly the diffusibility through the membrane of nerve tissue The longer lasting drugs diffuse at a slower rate than the shorter acting In addition, the longer lasting drugs are not as easily washed from the surface of

nerves after contact. Tetracaine is washed off with more difficulty than procaine.

Slight modifications and alterations of the molecular structure modify the pharmacologic action of a compound. For example, substituting a methyl group for the ethyl on the nitrogen atom of ethanolamine in procaine and a butyl radical for a hydrogen atom on the amino group on the aromatic nucleus results in *tetracaine* (Table VI). The potency is increased ten fold by this structural modification. On the other hand, merely removing the methyl group from ecgonine in cocaine nullifies the anesthetic activity.

### Toxicity

Toxicity, like potency, is a function of and varies with chemical structure. Two types of toxicity are recognized. *General or systemic toxicity* and a *local or tissue toxicity*. Systemic toxicity is discussed subsequently. Local toxicity is of extreme importance from a clinical standpoint. The action of clinically useful drugs is reversible. The function and structure of cells exposed to these drugs revert to normal upon removal. Drugs which do not possess this reversibility of action cause damage to both the nerve and the surrounding tissues. Dibucaine, quinine, and its derivatives have been reported to be locally toxic. Neurolysis and slough of tissues surrounding a nerve have occurred. Evidence exists that continuous application of a drug to a nerve induces changes which are slowly reversed or are irreversible. Local toxicity increases as the concentration of a drug increases. Local toxicity varies with the mode of administration of the drug and the nature of the cells into which it is injected. The so-called *long lasting local anesthetics* act by neurolysis rather than by physiologic blockade. Alcohol, phenol and oily solutions of bromsalizol or procaine, and other drugs are called long lasting local anesthetics, actually they are not local anesthetics in the sense in which the term is used.

## TYPES OF BLOCKS

The duration of action depends upon a number of factors. Among the most important are the concentration of the drug, the nature of the tissues into which the injection is made, the blood supply of the injected tissues, and the size of the nerve fibers coming into contact with the drug. To be effective, a local anesthetic drug must come into direct contact with nerve tissue. All types of nerve tissue are susceptible. The drug acts by preventing conduction in a nerve unit. Whether applied to the cell body or to the nerve axones or dendrites the physiologic response is the same.

Clinically, a local anesthetic drug is applied at one of the following sites. In the subarachnoid space (*spinal block*), in the epidural space (*epidural block*), on a spinal nerve, paravertebrally (*paravertebral block*), along the course of a peripheral nerve before it branches (*nerve block*), to several

branches as it is dividing (*field block*), and to the nerve endings themselves The application to nerve endings is either by injection over a wide area (*infiltration*) or by application on a mucous membrane in which the nerve endings are distributed (*topical*) Local anesthetics are without effect when applied to the unbroken skin, because of their inability to penetrate the horny layers

## Diffusibility

The number of fibers in a nerve bundle which are blocked by a drug varies with the technique of application Several factors combine to cause this variation, the chief one is the power of penetration In the epidural space, the spinal nerves are sheathed with a covering which is continuous with the dura The concentration of procaine necessary to cause a complete blockade of all fibers must be approximately ten times that necessary to block the naked roots in the subarachnoid space Half per cent solutions of procaine are adequate for the endings of the peripheral nerve for which infiltration techniques are used This concentration, however, is too dilute to penetrate the larger peripheral nerves and nerve trunks These are thicker and have a sheath A 1 5 or 2 per cent solution must be used to interrupt conduction in these Once the blockade is established it remains in effect until there is restitution of the fiber to normal As the drug action disappears and restitution progresses to the point where conduction is resumed, the impulse passes through the affected area without decrement There is no depth of anesthesia in conduction anesthesia A fiber either conducts or does not conduct

Certain drugs readily penetrate mucous membranes and are excellent for topical anesthesia Others either penetrate slowly or are carried away so rapidly from the mucous surfaces that they are ineffective Procaine, unless used in exceptionally high concentrations, is not satisfactory for topical anesthesia Cocaine, tetracaine, piperocaine, dibucaine, hexylcaine, and lidocaine serve well for this purpose however

## Effect of Fiber Size and Drug Concentration on Blockade

Along with penetrating power, size of nerve fibers is an important factor It is well established that sensory and autonomic fibers of a mixed nerve are affected before the motor fibers This behavior formerly was attributed to a supposed difference in structure and in composition of nerve fibers Now it is recognized that the difference is due to fiber size

Sensory and autonomic fibers are smaller than motor They are more susceptible to and are affected first by the drug because they are smaller Nonmyelinated fibers are affected before myelinated ones, and myelinated nerves without sheaths before those with sheaths Drug concentrations ordinarily used clinically effect all three types of fibers, but not simultaneously There

is a latent or lag period from the moment the drug is applied until the full effect is obtained During this time the blockade is being established However if solutions are sufficiently dilute, the majority of sensory fibers may be blocked without involving the motor fibers In differential spinal block a dilute solution of procaine (02 per cent) is infused continuously into the subarachnoid space at a slow rate (1 cc per minute) through a catheter Blockade of sensory and autonomic fibers is obtained Perception of light touch pain and temperature is lost Perception of deep touch, pressure, position sense, vibration sense, and motor power remain intact

In the conventional type of spinal anesthesia using minimal doses, all of the fibers in the nerve roots in the vicinity of the needle puncture are affected—motor sensory, and autonomic The greatest concentration of drug is in the lumbar area and the drug is sufficiently concentrated to block all types of fibers In the thoracic region the solution is more dilute and the larger fibers are not affected Little if any motor blockade is present The sensory anesthesia and autonomic blockade, however are well established When larger than minimal doses are injected, there is an increase in concentration of drug in the areas removed from the puncture site and an increase in the number of fibers blocked All fibers are then involved Motor blockade then is established If a nerve is subjected to a graded increase in concentration of a solution, an optimal concentration will be attained which is capable of blocking all instead of certain groups of fibers in a mixed nerve. This concentration is the therapeutic concentration Increase in the concentration beyond this point has little if any effect on the blockade Evidence exists that irreversible changes may occur when so-called therapeutic concentrations are exceeded The possibility of systemic reactions is also increased The autonomic blockade and the motor paralysis are responsible for the physiological disturbances, particularly those of the cardiovascular system, which occur during spinal and epidural anesthesia. The toxicity and potency of the drug have little to do in initiating these changes, if the usual anesthetic concentrations are used

## Intensity of Anesthesia

Relatively less potent drugs such as procaine or piperocaine employed for block anesthesia allow greater leeway in the estimation of doses than drugs of high potency An error of 1 mgm in estimating the dose of tetracaine is comparable to one of 10 mgm of procaine The physiologic disturbances caused by conduction anesthesia depend upon *intensity of anesthesia* The intensity of anesthesia refers to the number and types of fibers in a mixed nerve which are blocked i e to the completeness of the block. The maximum intensity is obtained when there is complete sensory motor and autonomic blockade Intensity depends upon dosage and dosage in turn depends upon potency

Physical agents, such as cold and pressure, induce the same effects as chemicals and cause a blockade also Prolonged use of such physical agents results in permanent damage to the nerve

## Duration of Action

Duration of action, as has been mentioned previously, depends upon chemical structure Variable factors, such as the mode of administration, concentration, and duration of contact with the nerve, further influences duration of action In man procaine intrathecally blocks conduction for 40 to 60 minutes The same drug injected intradermally in identical concentrations causes anesthesia for an average of 15 minutes The addition of vasoconstrictors prolongs the action and reduces the toxicity by retarding absorption of the procaine from the injection site Procaine is the standard of comparison for drugs used for infiltration, nerve blocks, and spinal anesthesia Cocaine is the standard for comparing drugs used for topical anesthesia

Potent drugs such as tetracaine, dibucaine, and eucupine are characterized by prolonged action Establishment of a blockade using longer acting drugs requires more time than the shorter acting drugs Procaine intrathetically causes a blockade of all fibers in the posterior and anterior roots within two or three minutes Under comparable circumstances, tetracaine blocks completely within five to seven minutes, dibucaine in approximately seven to 10 minutes Hypalgesia appears first, then in the following order there is loss of perception of light touch, pain, temperature, vibratory sense, position sense, and deep pressure Sensory anesthesia in turn is followed by motor paralysis With all drugs there is a latent period from the moment of injection until a blockade is established The latent period is shortest for the shorter acting drugs As long as ten minutes may elapse before anesthesia is established when using a long lasting drug such as tetracaine This latent period is shortened as the concentration of drug is increased When spinal anesthesia is induced using dibucaine or tetracaine, hypalgesia is established promptly but complete insensibility is delayed several minutes Therefore, in order to establish the desired level using long lasting drugs one seeks the areas of hypalgesia rather than anesthesia during the sensory examination

## Potentiation of Action

Substances may be combined with local anesthetics to potentiate their action Potassium salts (the K ) enhance the effect of procaine However infiltration of tissues with solutions containing potassium salts causes pain, edema, and redness in the post anesthetic period Proteins also potentiate local anesthetic action Gliadin, human plasma, and serum albumen added to procaine prolong its effect The increase in duration is not remarkable from a clinical standpoint and the benefits derived are not worth the trouble entailed in preparing the solutions Alkalinization of solutions of anesthetic

drugs has been recommended to enhance the local anesthetic effects, but the procedure is of doubtful value The free base is the agent which penetrates into the cell and causes the physiologic change and not the salt Regardless of the pH a solution may have before injection, it becomes adjusted to the pH of the tissues after injection by virtue of the buffer action of the electrolytes in the tissue fluids Most solutions used clinically are acid in reaction because they are prepared from the salts Their pH is raised to that of the tissues, likewise the pH of alkaline solutions is lowered to that of the tissues Potentiation by alkalinization occurs when a drug is applied topically, but in present day practice the procedure is only rarely used

## Use of Vasoconstrictors with Local Anesthetics

Vasoconstrictors are incorrectly classed as potentiating agents They decrease the toxicity and prolong the action by causing local ischemia The most efficient drug in the entire group of vasoconstrictors is epinephrine Ephedrine, neosynephrine, and related amines are nowhere near as effective Norepinephrine (arterenol) is almost as effective as epinephrine, but its use is not advised because the extreme vasoconstriction has caused gangrene Vasoconstrictors are used in highly vascular areas such as the scalp Their use is not advised for nerve blocks performed on the digits, particularly when peripheral vascular diseases are present The usual effective concentration of epinephrine varies between 1 10,000 and 1 200,000 Most clinicians use more than is necessary Tachycardia, hypertension, tremor, pallor, and other distressing symptoms of sympathetic stimulation invariably appear, particularly when an excess of epinephrine is used These symptoms are often confused with those of a reaction to the anesthetic drug It is needless to say that epinephrine should be omitted when regional anesthesia is used for patients who have cardiovascular disease, hypertension, hyperthyroidism, and similar clinical conditions in which sympathetic stimulation might be undesirable

## Methods of Assay and Testing

There are a number of methods for testing the potency and efficiency of local anesthetic drugs The drug may be applied topically to the cornea or on mucous membranes of animals or man It may be injected intradermally into the skin of animals and man or it may be applied directly to nerves in the spinal cord of animals These are some of the techniques which have been used to investigate the efficacy of these drugs The results of such studies cannot be compared unless the experimental data are obtained under identical conditions

## Systemic Toxicity of Local Anesthetics

In the last analysis the value of a local anesthetic drug is determined

by its toxicity Irrespective of the manner of administration, a local anesthetic ultimately gains access to the blood stream Toxic manifestations do not appear until a certain blood level has been attained and exceeded This value differs for each drug and depends upon its diffusibility in tissues, potency, toxicity and ease of elimination Only minute traces of certain highly toxic drugs need be present in the blood to cause untoward symptoms The blood level is dependent upon the rate of absorption from the site of injection, and the rate of disappearance from the blood The latter depends upon the rate of detoxification or elimination and the capacity of tissues to store the drug There is evidence that procaine is stored to a limited extent in the muscles

The rate of absorption from the injection site depends largely upon the vascularity of the tissues and the concentration employed Absorption is rapid from tissues and areas abundantly supplied with blood vessels as, for example, the scalp Absorption is rapid from all mucous membranes, but particularly those of the respiratory tract, the lungs, urethra, vagina, and stomach Minute amounts of the drug circulate in the blood for some time after injection into the tissues During infiltration anesthesia with procaine, an increase in the pain threshold of the skin over the forehead has been demonstrated Presumably this effect is due to the absorption of the drug from the injection site and the widespread distribution to nerve endings in the tissues by the blood Certain drugs are unfit for clinical use because the amount absorbed from the injection site, even though minute, is sufficient to cause systemic reactions as it circulates in the blood stream The potency of a local anesthetic drug and the toxicity do not necessarily parallel each other The toxicity of a drug in comparison to its potency is an important value, but unfortunately it is a difficult one to establish in man The lethal dose is established by injecting the drug intravenously at a given rate and concentration into animals and making comparisons with a standard Such data, though not directly applicable to man do, however, serve as a guide to the possible behavior in man Unlike other central nervous system depressants, species differences are not as great or as variable in studies of local anesthetics The clinical usefulness and safety of a new local anesthetic drug can be established only by its cautious repeated use by careful observers

## Absolute Toxicity and Relative Toxicity

Two terms which are frequently encountered in medical writings are "absolute toxicity" and "relative toxicity" Under comparable circumstances, 1 mgm of tetracaine is as lethal as 10 mgm of procaine The absolute toxicity of tetracaine compared to procaine is 10 However, the potency of tetracaine is 10 times that of procaine One tenth the amount is necessary to establish anesthesia Relatively, then, the toxicity of tetracaine equals that of procaine Duration of action is not taken into consideration in expressing

this value Relative toxicity is a comparative value which takes into account the potency along with the intravenous toxicity on a milligram for milligram basis

## Central Nervous System Type of Toxic Reaction

Two types of systemic reactions to local anesthetic drugs are recognized, the *central nervous system type* and the *cardiovascular type* Such terms as "sensitivity," "idiosyncracy," and "hypersensitivity" are frequently used to describe reactions but they are meaningless Almost without exception reactions due to overdosage result from injection of an excess, or from the use of concentrated solutions, or rapid intravascular injection The symptoms in all types of reactions are referable to three physiologic systems, the nervous system, the respiratory system, and the circulatory system

When the drug affects the central nervous system primarily, two phases may be recognized in a toxic reaction—one of *stimulation,* which usually appears first, and one of *depression* or paralysis If the dose is overwhelming for the individual, the phase of stimulation may be unnoticed or does not appear Most local anesthetic drugs stimulate the central system from above downward Small doses intravenously increase the sensitivity of the cerebral cortex to electrical stimulation Convulsions occur more consistently in species having higher degrees of cortical development Increased mental keenness, talking excitement, and vomiting are the prodromal signs of such stimulation in man These are usually passed off as "hysteria" or apprehension by uninitiated physicians Convulsions then appear If the drug continues to be absorbed depression or paralysis of the central nervous system follows When the medulla is stimulated, variations in blood pressure and in the respiratory pattern occur Respiration may increase in both rate and depth A rise in blood pressure is first observed due to stimulation of the vasomotor center As absorption proceeds depression of the medullary centers follows characterized by respiratory failure and circulatory collapse The train of symptoms, the severity, and the order in which they appear varies with the drug and the rate of increase in the blood level Rapidly developing medullary paralysis causes respiratory failure Reactions characterized by syncope, often termed *idiosyncrasy* are believed to be due to sudden respiratory failure During the convulsive phase the muscle spasm may interfere with pulmonary ventilation

The following sequence of events occurs in animals when the central nervous system is stimulated by toxic doses of drugs injected intravenously Respiratory stimulation, elevation in blood pressure followed by a depression below the control level, slowing of the heart probably due to myocardial depression, then an improvement of the heart beat with an increase in blood pressure, then respiratory paralysis followed by convulsions In man the sequence of events is different Usually the central nervous system stimu

lation accompanies or even precedes the circulatory and respiratory effects Excitement and apprehension following the application and injection of a local anesthetic drug in an otherwise calm patient should be viewed with suspicion Excess procaine causes convulsions, excess tetracaine more frequently causes sudden syncope due to cardiac failure and respiratory paralysis rather than convulsions, cocaine causes excitement and convulsions most frequently, lidocaine induces a drowsy sleepy state with some disorientation or amnesia when an excess is absorbed slowly, convulsions when it is absorbed rapidly However, the type syndrome which develops depends upon the rate of absorption, the amount absorbed, and the status of the patient

## Vascular Type of Reactions

The vascular type of reactions are due to cardiac depression A decrease in cardiac output may follow In addition, a local vasodilatation may occur particluarly when large amounts are used Hypotension results Combined vasodilatation and myocardial depression may occur giving rise to hypotension Sudden deaths following the injection of minute amounts of local anesthetics which have been ascribed to *idiosyncrasy* are probably due to circulatory collapse A few drugs cause vasoconstriction locally Cocaine and to a lesser extent monocaine have this action Bradycardia may be noted when the vagus center is stimulated in the central nervous system type of reaction Stimulation of the vasomotor center may cause an elevation of blood pressure

## Allergic Reactions

Allergic responses to local anesthetic drugs are uncommon although many reactions due to overdosage are called allergic The possibility of an allergic reaction is more remote if the patient has never been exposed to or received a local anesthetic drug previously Interaction between a local anesthetic and the tissue proteins may form antigens which give rise to antibodies Subsequent exposures result in manifestations of allergy Allergic manifestations to local anesthetic drugs follow repeated use of the drug rather than single exposures The responses are seldom immediate Usually they are delayed, somtimes for hours Seborrhea, eczema, and other cutaneous manifestations are the most common responses Systemic reactions such as bronchial spasm, urticaria and dyspnea may occur and have been reported It is doubtful that deaths occurring unexpectedly during local anesthesia can be classed as being due to anaphylactic reactions or due to allergic responses Allergy to local anesthetics is more often an occupational disease Dentists and physicians are commonly afflicted

## Intolerance

Intolerance to local anesthetics is an uncommon finding Patients respond in a normal fashion to smaller than the usual quantities of a given drug

Symptoms of a severe reaction ensue when ordinary doses are injected in these subjects Such behavior is erroneously termed "idiosyncrasy" or "sensitivity" Actually it is due to overdosage pure and simple

## Testing for 'Sensitivity"

Skin tests to determine "sensitivity" in order to avoid toxic manifestations of local anesthetic drugs are of little or no value In spite of this many clinicians rely upon them and perform them routinely Two intradermal wheals are raised using the solution in question for one and normal saline for the other The latter serves as a control Areas of erythema or pseudopod formation are presumed to be evidence of "sensitivity" whatever that might be Convulsions, syncope, and other manifestations of toxicity have been known to develop when the test was judged "negative"

One test which is of more value and has a more logical basis is the *intranasal test* This is actually a test for tolerance Control readings of pulse and blood pressure are taken with the patient in the supine position until a base line is established One drop of the drug to be tested is instilled into one nostril and pulse and blood pressure are noted several times during the next several minutes If no untoward reactions are noted two additional drops are instilled After three minutes, four drops, then eight, then 16, then 32 If no changes in pulse, blood pressure or excitement appears, intolerance may be presumed not to be present

## Relationship of Toxicity to Detoxification

Toxicity bears a direct relationship to ease of elimination Local anesthetic drugs are either eliminated unchanged in the urine, detoxified by the liver, or are detoxified partly and partly eliminated unchanged As a rule drugs which are slowly destroyed or are eliminated unchanged are more toxic than those which are easily and rapidly detoxified The exact fate of many of the numerous available drugs has not been determined as yet It is more than likely that, since they are esters, they are hydrolyzed into their respective acids and alcohols More is known concerning the fate of procaine than any of the other drugs

Procaine is first hydrolyzed to paraminobenzoic acid and diethylamino ethanol The paraminobenzoic acid is either conjugated with glycine to form benzoyl glycine or it is methylated to form methylparaminobenzoic acid Cocaine *is partly detoxified Ecgonine and benzoic acid are the detoxification* products Some cocaine is recovered unchanged in the urine The rate of detoxification of a local anesthetic drug may be retarded if liver insufficiency is present *Intolerance* may be explained by this fact Less concentrated solutions should be used for subjects in the older age groups because they may detoxify the drug at a slower rate than younger subjects

## Antagonism to the Stimulating Action

The stimulation of the cerebrum and sub cortical structures is antagonized by central nervous system depressants Non volatile substances such as chloral, paraldehyde, tribromoethanol, and the barbiturates are more effective and preferred to the volatile drugs The barbiturates are superior to other depressants in this respect Barbiturates are suitable only for overcoming convulsions They are of no value in treating the paralytic phase of a local anesthetic reaction In fact the situation is made more serious if they are used in the depressed phase Likewise, they are of no value in the cardio vascular type of reaction Short acting barbiturates are preferred to the long or intermediate, inasmuch as the latent period is shorter and they are more potent In the order of decreasing efficiency are thiopental, secobarbital, pentobarbital, amobarbital, dial, phenobarbital and barbital Ultra short acting barbiturates are preferred above all others but are used less frequently because they are not always available in solution for immediate use Short acting barbiturates are used more frequently for office anesthesia because they are available for immediate use in solution in sterile ampules Prophylactic use of a barbiturate does not insure against a reaction, but does minimize or modify one, should it occur

## Prevention of Reactions

One should observe the following precautions in using local anesthetic drugs (1) Use the least possible quantity of the most dilute effective solution (2) Use the least toxic drug for the purpose (3) Attempt aspiration before each injection and ascertain that the needle is not in a vessel to avoid intravascular injection (4) Add epinepherine to the solution, particularly when infiltrating highly vascular areas (5) Allow sufficient time to elapse between sprays when using drugs topically (6) Use a barbiturate for pre anesthetic medication

## Management of Reactions

The treatment of toxic reactions is largely symptomatic For excitement without convulsions, sedation with a barbiturate intravenously is indicated and is usually sufficient treatment If convulsions are present, an ultra short acting barbiturate intravenously in amounts sufficient to control them is the best choice If an ultra short acting barbiturate is not available, a short acting derivative may be used, bearing in mind that a latent period of several minutes exists from the moment of injection until the depressant action is established If the paralytic phase of a reaction has occurred, artificial respiration is immediately instituted by whatever method is available (Do not inject a barbiturate ) Hypotension, regardless of its etiology, in a reaction is overcome by the use of a vasoconstrictor drug Ephedrine 25 mgm , desoxyephedrine 5 to 10 mgm , or neosynepherine 0 5 mgm initially followed

by additional amounts as required are given intravenously Fluids are in effective for combating this type of response If cardiac arrest is suspected or has occurred, massage of the heart together with artificial respiration must be instituted immediately Epinephrine injected into the right auricle may be necessary under such circumstances If the patient has lapsed into a coma tose state without circulatory collapse or respiratory failure, nothing but "watchful waiting" is necessary The use of stimulants is not advised be cause they behave like local anesthetics—stimulate first and depress after ward They would therefore contribute further to any existing depression Analeptics such as metrazol, coramine, and picrotoxin have no place in the treatment or management of reactions due to local anesthetic drugs

In local anesthesia prevention of reactions is simpler than cure

## REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 82

ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 200

ADRIANI J Local and Regional Anesthesia for Minor Surgery *Surg Clin North America* *31* 1507 1951

BEECHER H K *The Physiology of Anesthesia* New York Oxford 1938

COHEN E N and KNIGHT R T Hydrogen iron concentration of the spinal fluid and its relation to spinal anesthetic failures *Anesthesiology* *8* 594–600 1947

HIRSCHFELDER A D and BIETER Local Anesthetics *Physiol Rev* *12* 190 1932

HOMEYER W MINTZ S ADRIANI J The effects of the duration of spinal anesthesia of combining non anesthetic substances with the agent *Anesthesiology, 13* 231–241 1952

ORKIN L R ROVENSTINE E A Hexylcaine (Cyclaine) usefulness in regional and topi cal anesthesia *Anesthesiology* *13* 455–465 1952

RUPP R E Modern concepts of refrigeration anesthesia. *Anesth & Analg* *22* 18 1943

WEBB A M and BLAIR H A The action of procaine on the heart *Anesthesiology, 12* 261 1951

# XI

# LOCAL ANESTHETICS (CONTINUED)

## CLINICAL USES

### Intravenous Procaine

A recent medical fad which is rapidly losing its popularity is the intravenous use of procaine Extremely dilute solutions of local anesthetics may be infused slowly intravenously The less toxic drugs are withdrawn from the blood stream and are stored in the tissues or detoxified The blood level is thus kept at a minimum and a "reaction" does not occur Acceleration of the rate of administration causes a rapid rise in blood levels and symptoms of toxicity then appear Procaine may be infused by continuous drip (0 1%) at the rate of 1 gram per hour without any untoward manifestations The practice is not without hazards, however Circulatory collapse from myocardial depression and peripheral vasodilatation may occur when excessive quantities are used Intravenous procaine has been suggested as a therapeutic measure for a multitude of clinical conditions and painful syndromes Supposedly its effects are two fold (1) it acts as an analgesic, (2) it causes vasodilatation and improves the blood supply to a diseased structure It has also been advocated as a cardiac depressant in certain irritable states induced by cyclopropane, vagal reflexes, or manipulation of certain viscera The consensus among discreet, careful observers is that intravenous procaine (and also other local anesthetics) is of doubtful value The situations in which it is indicated and is of benefit are few and far between

### Spinal Anesthesia

#### PRINCIPLES OF SPINAL ANESTHESIA

Spinal anesthesia is induced by injecting a solution of a local anesthetic drug of proper strength into the subarachnoid space The anterior and posterior roots of the spinal nerves are blocked as they emanate from the cord There is little effect on the cord itself The neurons and tracts at the surface may be affected by the drug, but the ascending and descending tracts in the substance are not blocked If a small volume of a dilute solution of a local anesthetic is deposited at the thoracic segments by a technique known as *segmental spinal block* the lower extremities remain active The areas served by the thoracic nerves are blocked The extent of the block, often referred to as "height" or "level" depends upon the number of spinal roots bathed by the solution When the sacral segments only are involved, the perineal area (or

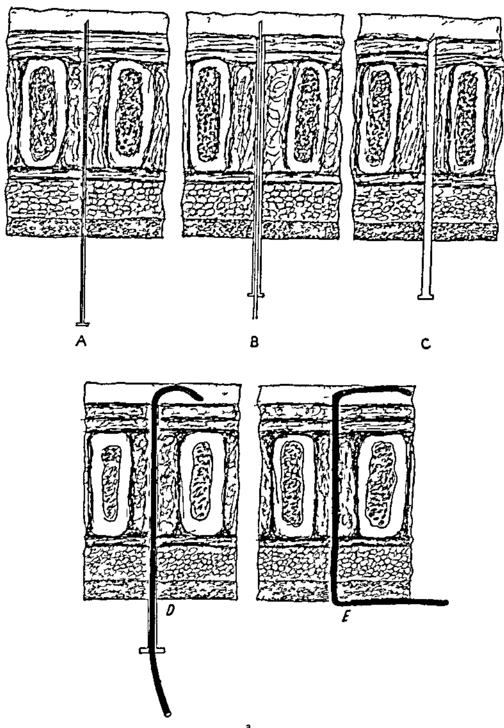
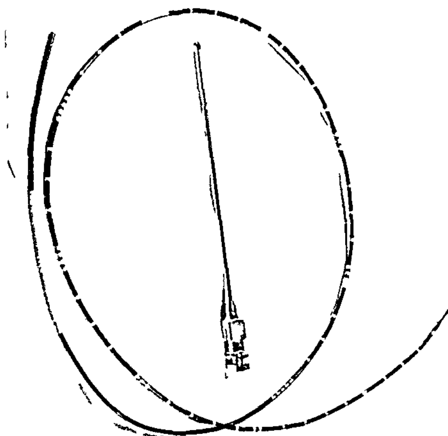



FIG 14 a Continuous spinal anesthesia Special spinal needle through which a fine catheter is introduced into the subarachnoid space After the catheter is placed at the desired spinal segment the needle is withdrawn The catheter remains behind the skin unsupported b Photograph of the catheter ordinarily used for continuous spinal anesthesia together with a Tuohy needle Plastic catheters may be used in place of the fine gauge ureteral catheters shown The needle has a special tip known as the Huber point



b

saddle area) is anesthetized The block is called *saddle block* When both the sacral and lower lumbar segments are involved, the lower extremities are anesthetized The block is referred to as *low spinal block* When the sacral, lumbar, and lower thoracic segments are blocked, the block is referred to as *medium spinal* block or simply *spinal block* If the drug is forced upward and bathes the upper thoracic segments the block is called a *high spinal* block The spinal cord ends between the second and third lumbar vertebrae Lumbar puncture is performed below this site, whether a "high" or "low spinal" is desired, to avoid trauma to the cord

Site of puncture, as a rule, has no significant relationship to the extent of anesthesia The distribution of anesthesia depends upon the number of spinal roots with which a given concentration of drug comes into contact The intensity depends upon the concentration bathing a nerve root Both extent and intensity depend upon the amount used Duration depends upon potency of the drug, it is dependent upon dosage only to a limited extent Anesthesia using procaine, intracaine, and piperocaine lasts an hour in most

instances, tetracaine and hexylcaine two hours, dibucaine, approximately three hours Duration is controlled by selection of drugs and not by varying the dose The extent or level is controlled by dosage and variations in technique Epinephrine added to solutions of spinal anesthetic drugs increases the duration of spinal anesthesia approximately 60 per cent Spinal anesthesia of long duration may be obtained by using a long lasting drug such as dibucaine combined with epinephrine by the single injection method

The *serial or continuous spinal technique* must be used if procaine or a drug of similar duration is selected In the latter technique, a catheter of small diameter is introduced intrathecally and the procaine is injected at repeated intervals as often as necessary (Fig 14) Originally the continuous spinal technique was executed by using a special mattress approximately 6 thick designed with a recess in the lumbar area A malleable needle was introduced into the subarchnoid space and was left in situ A rubber tube and a syringe were connected to the needle and the drug was injected at necessary intervals (Fig 15)

A technique called *differential spinal* block is useful for diagnostic purposes It is based upon the fact that a sufficiently dilute solution of a local anesthetic drug will block certain sensory fibers and not others A 0 2 per cent solution of procaine introduced through a catheter by the continuous

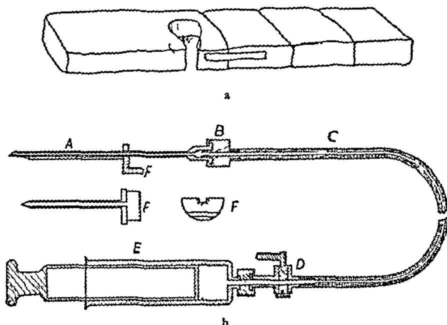



Fig 15 (a) The continuous spinal technique devised by Lemmon utilizes the special elevated mattress and malleable needle

(b) The assembly for continuous spinal anesthesia A is a soft malleable silver needle B is a lock for the needle C a thick walled rubber tubing D a two way stop cock E a 10 cc syringe for storing the solution F the top and side views of the introducer which is necessary to place the needle to keep it from bending as it passes through the tissues because it is malleable

drip method gives the differential blockade Ability to perceive light touch, pain, and temperature, are abolished Autonomic fibers likewise are blocked Pressure, vibratory sense, and motor functions are *not affected unless the* concentration of drug in the subarachnoid space is increased above 2 per cent

## Control of Extent of Anesthesia

Control of the extent of anesthesia is accomplished by using solutions which are heavier or lighter than spinal fluid A solution which is heavier than spinal fluid is referred to as *hyperbaric* A solution which is lighter than spinal fluid is termed *hypobaric*, one having a specific gravity equal to that of spinal fluid is called *isobaric*

*There are six extrinsic* factors involved in controlling the extent and intensity of spinal anesthesia These are (1) The dose of the drug, (2) the volume of solution used, (3) the site of injection, (4) the rate of injection, (5) the specific gravity of the solution, and (6) the position of the patient For consistent results when a certain level of anesthesia is required all factors are fixed *For example, for low spinal anesthesia using tetracaine,* 5 mgm of the drug are dissolved in 1 cc of 10 per cent dextrose This solution which is heavier than spinal fluid or hyperbaric, is injected rapidly (in two seconds) at the 3rd or 4th lumbar innerspace The patient is then placed in the supine position with the table tilted so that the head is up The technique remains the same at all times if this extent of anesthesia is desired Dosage, position, timing, rate of injection, volume, and specific gravity are not altered When a high level is desired, as far as the xyphoid for example, 10 mgm is used in a proportionate higher volume The patient is placed in the lateral prone position when the injection is being made and in the supine after the injection All six factors are maintained constant without variation The extrinsic factors can all be varied but the results will be inconsistent

The intrinsic factors are the diameter of the cord, the length of the cord, and the amount of spinal fluid surrounding the cord, the spinal fluid pressure and the pH of spinal fluid The anesthetist has no control over these factors

## Effects of Autonomic and Somatic Denervation

Spinal anesthesia provides muscle relaxation not obtainable with other types of anesthesia Too often surgeons demand spinal anesthesia for the relaxation it affords without regard to the patient's ability to withstand the effects of the block More occurs during spinal anesthesia than the readily apparent loss of sensation and muscle paralysis In high spinal anesthesia, there is a complete blockade of both sensory and motor fibers in the sacral, lumbar and the lower thoracic segments However, the autonomic fibers are not all blocked Both the sympathetic and parasympathetic components of the autonomic nervous system originating from the lower spinal segments

are inactivated In the thoracic segments, most of the sympathetic fibers are blocked The parasympathetic fibers, however, since they arise from the cranial nerves, particularly the vagus, remain intact

This partial denervation of the autonomic nervous system in the upper part of the body and complete denervation in the lower part, coupled with the somatic nerve paralysis, causes significant physiologic disturbances in unoperated individuals The disturbances become more complex when the physiologic changes are complicated by trauma, blood loss, traction reflexes, and other effects of surgery Mechanisms designed to compensate for these changes may not be effective in the presence of disease The disturbances, therefore are often enhanced when other conditions complicate the surgical diseases Some of the physiologic disturbances are of clinical significance, others are merely of academic interest It is important to understand the *physiologic changes which occur in order* to use spinal anesthesia safely In this discussion the changes of clinical significance will be emphasized

## Effects Upon Circulatory System

Of all changes which occur, those involving the circulatory system are the most important A hypotension is frequently associated with subarachnoid block It does not appear consistently, neither can one predict whether or not it will occur nor its severity should it occur Certain characteristics differentiate the hypotension from that caused by shock from trauma hemorrhage or reflex activity It develops shortly after induction of anesthesia, usually after the motor effects are established The systolic pressure falls slightly, but is usually well maintained unless the physiologic disturbances are severe The pulse pressure is decreased and a bradycardia is present if pre-anesthetic medication is omitted particularly if the block is a 'high spinal

The mechanism causing the hypotension is not completely understood It is well established that the circulation fails peripherally rather than centrally The fairly well maintained diastolic pressure, the lowered systolic pressure, the bradycardia and the diminished pulse pressure indicate that there is a decrease in stroke volume and that peripheral resistance does not change appreciably (Fig 16) Studies on cardiac output indicate a decrease Circulation time is prolonged in some cases it is doubled The arterial blood oxygen saturation remains unchanged but there is reduced venous blood oxygen content The arteriovenous difference is widened suggesting local tissue anoxia. Blood carbon dioxide content and serum carbon dioxide combining power are unchanged

Formerly it was believed that the blockade of sympathetic fibers with the concomitant arterial dilatation and pooling of blood in the peripheral and splanchnic vessels was the sole cause of the hypotension Arteriolar dilatation and pooling of blood does occur but appears to be confined to the peripheral vessels rather than in the vascular beds of the viscera This is

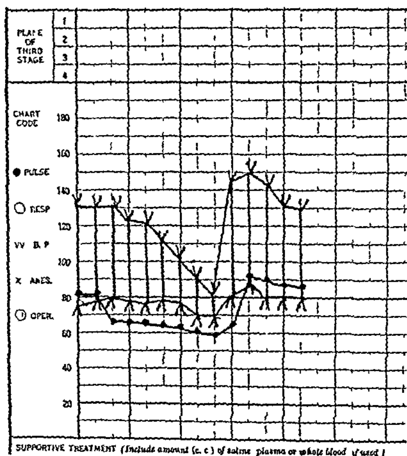



Fig 16 Typical blood pressure curve after the induction of high spinal anesthesia in an un premedicated patient A hypotension invariably results The hypotension is manifest immediately or shortly after the induction of anesthesia as soon as the blockade is complete Note the lowering in systolic pressure and the narrowing of the pulse pressure Diastolic pressure does not fall in proportion to the systolic and the pulse rate is decreased

borne out by the increases in skin temperature which occur, the absence of sweating in the anesthetized areas, and an increase in the volume of the limbs revealed by plethismographic studies Further investigation has shown that the splanchnic vessels do not dilate when sympathetic paralysis is induced There is an autonomous control, which is intrinsic, in the arterioles which maintains tone when denervation occurs When generalized dilatation of the entire or a sizeable portion of the vascular bed occurs, peripheral resistance is reduced A marked reduction of peripheral resistance is manifested by a lowering of the diastolic pressure Even though there is some reduction in diastolic pressure during spinal anesthesia, this is not remarkable and cannot be taken as an index of widespread vasodilatation Pooling of the blood in the peripheral vessels and in the spleen, which dilates two or three times its normal size contributes to approximately 10 per cent of the lowering of blood pressure There are other factors, which play a greater role in the lowering of the blood pressure, besides the dilatation caused by sympathetic paralysis

A factor, and one of the more important, is the decrease in venous return to the heart Return of venous blood depends upon three factors (1) the support and "milking" action of skeletal muscles upon the veins, (2) variations in the intra abdominal pressure which helps to propel the blood in the abdominal veins, and (3) variations in intra thoracic pressure which cause a negative pressure in the great veins During spinal anesthesia, most of the skeletal muscles are relaxed and return of blood to the heart is greatly retarded As the number of spinal segments anesthetized is increased, a greater mass of muscle tissue is denervated and the stagnation of blood in the veins of the muscles is increased in proportion In addition in high spinal anesthesia, the thoracic movements may be decreased due to paralysis of the lower intercostal muscles Hypotension, therefore, depends largely upon the level of distribution and the intensity of anesthesia

## Intensity of Anesthesia

Intensity of anesthesia refers to the completeness of the block There is a minimum concentration which causes a blockade of all fibers in a mixed nerve Below this minimum, some will be blocked and some will not, depending upon size The concentration may be reduced to a point which causes a blockade of sensory fibers only with no motor paralysis The greater the number of fibers blocked in a mixed nerve, the greater the intensity of anesthesia In upper abdominal surgery, the dose used must yield a concentration sufficient to block the motor fibers emanating from the lower thoracic segments if the upper recti are to be relaxed This concentration is more than is necessary to cause a complete blockade of all fibers below these segments Above these segments, there is a gradual diminishing or less intense area of anesthesia because the solution bathing these segments becomes more dilute An area will be reached in which there are only sensory and no motor changes (Fig 17) Dosage, therefore plays a role in causing circulatory derangements As the dose is increased the loss of motor activity is more

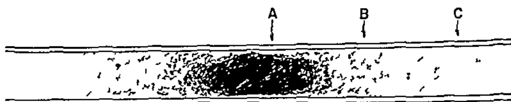



Fig 17 The manner in which the solution spreads after injection of a local anesthetic drug into the subarachnoid space The concentration becomes weaker both up and down the cord The dark areas (A) indicate a concentration sufficient to block all nerve fibers motor autonomic and sensory B shows the concentration sufficient to block only the sensory and autonomic fibers and possibly the smaller motor fibers C indicates the dilution which causes a complete blockade of the smaller sensory fibers and a partial blockade of the larger sensory fibers and autonomic fibers the motor fibers are not affected As the number of spinal segments requiring complete blockade is increased the dose must be increased otherwise the segments more remote from the puncture site will be only partially blocked

widespread The hypotension is often ascribed to toxicity of the drug, particularly when long lasting drugs such as tetracaine and dibucaine are used Actually it is *intensity of anesthesia* which is responsible The hypotension is no more severe with one drug than another when intensity and extent of anesthesia are the same The possibility of errors in estimation of dosage is greater when potent drugs are used, because a smaller quantity of drug is required Relatively speaking, and the possibility of error is greater with more potent drugs *An error in dosage of 5 mgm* of tetracaine is equivalent to one of 50 mgm of procaine

## Management of Hypotension

The hypotension is frequently referred to as "spinal shock" by some *clinicians* It differs in a number of respects from shock caused by trauma, hemorrhage, reflex stimulation, or other causes (Table VII) In spinal anesthesia, the hypotension is neurogenic in origin Blood volume, at the onset, is not appreciably disturbed Venous pressure is lowered at the arm veins Hemoconcentration is not a part of the picture The specific gravity of the blood and the hematocrit are not significantly altered The vascular bed is relaxed so that a disparity exists between its volume and the effective blood volume In shock from trauma or hemorrhage, both the cross sectional area of the vascular bed and *the blood volume are reduced Vaso*

TABLE VII

THE SIMILARITIES AND DIFFERENCES BETWEEN HYPOTENSIVE STATES OF NEUROGENIC ORIGIN AND THOSE DUE TO LOSS OF FLUID

| | Spinal Shock | Traumatic Shock |
|---|---|---|
| Systolic pressure | Decreased | Decreased |
| Diastolic pressure | Decreased slightly | Decreased |
| Pulse | Slowed | Increased |
| Pulse pressure | Decreased | Decreased |
| Venous pressure | Decreased | Decreased |
| Blood volume | No change | Decreased |
| Vascular bed | Dilated | Constricted |
| A V difference | Widened | Widened |
| Circulation time | Prolonged | Prolonged |
| Hematocrit | No change | Increased |
| Response to fluids | Poor *unless large amounts* are used | Responds |
| Response to vasopressors | Good | Poor usually harmful |

pressor drugs readily overcome the derangements caused by spinal anesthesia, presumably by decreasing the cross sectional area of the vascular bed. Fluids are ineffective unless they are administered rapidly and in large amounts. The reverse is true in hemorrhage and traumatic shock.

The hypotension of spinal anesthesia develops as soon as anesthesia and motor paralysis are established. Hypotension which develops after the operation has been in progress for a time is attributable to the surgery. It is corrected by the administration of fluids and does not, as a rule, respond to vasoconstrictors. The mechanisms responsible for circulatory adjustments are controlled by the autonomic and central nervous systems. They do not operate effectively during spinal anesthesia. Inhalation of carbon dioxide, which ordinarily causes the blood pressure to rise in unanesthetized subjects, has no effect upon the blood pressure during spinal anesthesia. In the unanesthetized area the skin is pale, the vessels are constricted and the temperature is reduced. The vasoconstriction present in this area is an indication of an attempt to overcome the circulatory derangements. In the anesthetized area in high spinal anesthesia, the sympathetic pathways are blocked but the vagal pathways are active. The pulse rate, therefore, becomes slow. Other manifestations of vagal activity are also present.

## Effect of Positional Changes

Hypotension is easily precipitated by positional changes because the compensatory mechanisms responsible for circulatory readjustments are disrupted. Care must be exercised in shifting positions or transporting patients from one locality to another. Since circulatory depression frequently follows shifting from the supine to the Trendelenburg, the lateral, the prone, and to other positions, patients should be moved with care or not shifted at all if possible.

## Contraindications to Spinal Anesthesia

Obviously when the circulatory system is impaired in any manner an anesthetic procedure which precipitates circulatory derangements, such as those which accompany spinal anesthesia, is best avoided. It is not uncommon for severe hypotension to develop after induction of spinal anesthesia in patients who have cardiovascular diseases, anemia, shock, dehydration and blood loss. Hypotension appears abruptly in these subjects, it is more severe and does not respond to vasopressor substances. It is common experience to find that vasopressor substances are least effective when needed most. Sympathectomized subjects do not tolerate even mild degrees of hemorrhage. Spinal anesthesia is best avoided when bleeding is anticipated unless provisions are made for immediate adequate blood replacement. Patients with increased intra abdominal tension from ascites, intestinal obstruction, marked gaseous distention, tumor masses of unusual size, or pregnancy

develop severe hypotension promptly after induction of spinal anesthesia The mechanisms causing it are not understood Most likely compression of the great veins in the abdomen interfers with the return of venous blood from the extremities to the heart

### Causes of Fatalities

Circulatory disturbances during spinal anesthesia cannot be disregarded If untreated cerebral anemia invariably develops, this is in turn followed by respiratory failure and cardiac arrest The majority of fatalities during spinal anesthesia result either from one of two causes (1) Severe, usually abrupt and uncontrollable, circulatory collapse, and (2) asphyxia due to ascent of the drug into the upper thoracic and cervical segments Paralysis of both the intercostal muscles and the diaphragm occurs and ventilation ceases Both complications may be averted by the proper selection of patients and exercising utmost care in inducing anesthesia The pulse, respiration, and blood pressure must be carefully and constantly observed during anesthesia Provisions for immediately instituting artificial respiration and overcoming circulatory collapse should be made before the spinal block is attempted No spinal anesthetic should be induced without having a respirator of a satisfactory type immediately available Cardiac arrest during spinal anesthesia is due to respiratory failure which results from cerebral anemia This in turn is due to peripheral circulatory failure or paralysis of the respiratory muscles from a high spinal anesthetic Idiosyncrasy to the drug, "toxic reactions," and other vague causes are responsible for few, if any, deaths

### Metabolic Effects

Metabolic disturbances accompany the hypotension during spinal anesthesia The widened arteriovenous difference and the prolonged circulation time increases the possibility of local tissue anoxia Spinal anesthesia uncomplicated by hypotension, has little effect on metabolic processes Liver function, blood glucose, non protein nitrogen, carbon dioxide combining power, and bleeding and clotting time are not significantly altered If a hypotension occurs and it is not corrected promptly, the impairment of liver functions may occur Glomerular filtration and tubular excretion and reabsorption are likewise not significantly affected by uncomplicated spinal anesthesia

### Effects on the Stomach, Intestines

The effects of spinal anesthesia upon smooth muscle of the viscera, particularly that of the uterus and intestine, are worthy of note The upper portion of the gastro intestinal tract, that innervated by the vagus, assumes a ribbon like contracted appearance when anesthesia extends to the thoracic

segments, and causes a sympathetic blockade The motor effects of the vagus then predominate Traction upon the mesenteries of the abdominal and pelvic viscera often cause discomfort because there is a retrograde transmission of impulses along the vagus or from one ganglia to the next in the sympathetic chains In upper abdominal surgery particularly, patients complain of pain in the chest, around the heart or in the neck On occasions, traction on structures in the biliary tract or on the diaphram causes pain in the shoulders This is due to retrograde transmission of impulses along the phrenic nerves, which like the vagi are active

### Effects on the Uterus

The effects of spinal anesthesia upon the uterus depend upon the number of spinal segments affected Sensory fibers enter the uterus from the sacral and lower lumbar segments, motor fibers from the thoracic segments Contractions are not inhibited if the blockade is confined to the lower spinal segments Blocking the autonomic fibers of the thoracic segments causes both the intensity and frequency of uterine contractions to diminish The uterus does not relax during spinal anesthesia, but maintains its usual tone Fetal blood oxygen and carbon dioxide content are not altered appreciably during spinal anesthesia, provided the blood pressure is maintained within the normal limits

## Complications During Anesthesia

Nausea and vomiting are not uncommon complications during spinal anesthesia Frequently, nausea occurs immediately after the solution is injected into the intrathecal space Whether or not this occurs reflexly when the chemical comes into contact with the nervous elements and the meninges, is not known On other occasions nausea and vomiting herald the onset of *hypotension* Presumably this is due to medullary anemia resulting from the circulatory depression Yawning frequently preceeds the vomiting Sometimes the *vasopressor drugs* used to overcome the hypotension cause nausea Some patients respond to ephedrine and neosynephrin in this manner *Traction on the viscera* may induce vomiting Narcotics such as morphine or demerol administered for sedation particularly intravenously, are sometimes responsible for nausea and vomiting The cause must be determined before proper treatment can be instituted If due to hypotension vasopressors and inhalation of oxygen are indicated If due to traction reflexes, supplementary inhalation anesthesia may be necessary to overcome it Sedation and hypnosis with a slow intravenous drip of a dilute thiopental solution usually controls nausea of reflex origin or that due to drugs Dramamine intravenously is sometimes effective when other forms of therapy fail

## Post Anesthetic Complications

### Neurological Complications

Some of the most dreaded complications of spinal anesthesia are the palsies and paraplegias which are said to follow it Fortunately these are rare, but they are distressing and disabling when they occur Neurologic complications occurring after spinal anesthesia are (1) headache, (2) cranial and other nerve palsies, (3) paraplegia and other afflictions of the cord due to myelitis, trauma, and other factors, (4) infections of the meninges due to bacterial contamination, and (5) sterile inflammation of the meninges due to drugs

#### Headache

Headache following lumbar puncture is distressing and annoying, but is neither dangerous to life nor permanent Much has been written concerning its etiology The available evidence indicates that the loss of cerebrospinal fluid from the perforation of the meninges made by the needle is the causative mechanism The use of small gauge needles has been advocated to reduce the incidence of headache These headaches are characterized by a reduced spinal fluid volume Some headaches are reflex in origin or are due to meningeal irritation (meningismus) from chemical irritation by the drug These are often associated with an increased spinal fluid pressure The incidence of headache apparently is higher in obstetric patients because the alternate increase and decrease of intra abdominal pressure is transmitted to the peridural veins via the abdominal veins The spinal fluid pressure is increased with each uterine contraction causing a milking action around the arachnoid A loss of fluid then results The cerebral spinal fluid pressure is zero in cases in which the etiology is loss of fluid

Certain characteristics differentiate post lumbar puncture headache from other types Usually the headache appears within the first twenty four hours It is throbbing in character, and is distributed behind the orbits, over the frontal area, and sometimes in the occipital region Occasionally it is confined to the cervical area in the back of the neck Nausea may be present It is aggravated by a change in position, particularly when the patient sits up after reclining The type due to meningeal irritation with increased pressure is ordinarily confined to posterior aspect of the neck rather than to the head although it is possible for pain to be present in both the head and neck, the back or even the legs No fever is associated with post spinal headache Ordinarily a headache lasts three or four days and then gradually recedes In more persistent cases it may last ten days or more Obstinate cases have been known to last for months, however, this is uncommon

The various therapeutic procedures which have been suggested for relief of headaches are directed towards restoring to normal the hydrodynamics

of the cerebral spinal fluid Hypotonic solutions are administered to promote the secretion of cerebral spinal fluid Preoperative hydration by "forcing" fluids has been suggested to accomplish the same purpose Drugs which decrease urinary output, such as pituitary extract, or drugs which cause retention of fluid, such as the hormones of the adrenal gland, have been advocated Direct replacement of the fluid in the subarachnoid space by injection of normal saline promptly relieves the headache for periods of several hours to days or even permanently The injection must be repeated a number of times before complete relief is obtained The peridural injection of saline has been advocated also and has met with some success The intracaudal injection of 25 to 30 cc of saline is as effective as the peridural injection Usually one or two injections at 12 to 24 hour intervals will suffice Vasodilating drugs have been administered to increase the blood flow through the choroid plexus, thereby increasing the formation of cerebro spinal fluid Nicotinic acid and the nitrites are drugs with such an action Intravenous alcohol likewise has been advocated as both an analgesic and as a vasodilator None of these aforementioned measures has yielded dramatic results Each has at various times proved partially or completely successful

PALSIES

Palsies of the cranial nerves are also associated with loss of cerebrospinal fluid The nerve most commonly involved is the sixth or abducens Several days after the spinal anesthetic the patient complains of diplopia Often the diplopia is associated with post lumbar puncture headache The exact etiol ogy of the nerve injury is not known Perhaps when the volume of spinal fluid is reduced, the cushioning effect at the base of the brain is lost The pressure of the brain upon the base of the skull and the ensuing traction of the dura causes pain In addition this shifting about causes traction on the cranial nerves, and, since the sixth nerve is one of the longest and the slender est of cranial nerves it is more subject to trauma than the others The diplopia lasts anywhere from several weeks to months It is usually not permanent

Dizziness and deafness are also associated with a loss of spinal fluid Direct connections exist between the labyrinth and the subarachnoid space Loss of spinal fluid also causes disturbances of fluid pressure in the labyrinth Symptoms of eighth nerve involvement may also occur, although they are uncommon Palsies of other cranial nerves and any of the spinal nerves may occur but are rare Their etiology is not easily explained Differentiation must be made between the neurologic changes due to pressure upon nerves from positioning and those of central origin

The most serious complication of spinal anesthesia is a paraplegia, often called the "cauda equina syndrome" The latter term has been adopted because the symptoms are referable to the area supplied by the nerves com

posing the cauda equina The onset and symptoms of the "cauda equina syndrome" follows no set pattern In some cases the spinal anesthetic is induced successfully and is uneventful during the operation, but the block merely fails to disappear within the usual time The patient remains paralyzed In others, the patient complains of excruciating pain as the drug is injected Shock and coma follow from which the subject recovers hours later with a fully established paraplegia In others the patient is returned to bed apparently in good condition Several hours later shock with coma supervenes, from which the patient recovers with a paraplegia And still in others the patient recovers fully from the anesthetic, and days later gradually notices weakness numbness and other sensory changes in the extremities The neurologic changes gradually become worse until paralysis is complete Foster Kennedy has described a chronic arachnoiditis presumably associated with spinal anesthesia In cases which came to his attention the symptoms did not appear immediately as has been the case in most cauda equina syndromes, but began anywhere from six months to a year after the spinal anesthetic had been administered Whether or not the spinal anesthetic was incidental to a slowly developing arachnoiditis or whether it was a causative factor is difficult to say Thus far, Kennedy appears to stand almost alone in associating chronic arachnoiditis with spinal anesthesia

Irrespective of the manner in which the syndrome begins, ultimately the patient becomes paralyzed below the waist, develops fecal and urinary incontinence, contractures atrophies, and other manifestations of degeneration of the cord The symptoms may gradually recede after a few weeks and the patient recovers both motor and sensory function In others it persists, or may even become worse for several weeks and then remains stationary As a rule the paraplegias which fail to show improvement after five or six months are permanent Recovery if it occurs is usually complete within five or six months After that time the prognosis is poor Fortunately this complication is rare In thirteen years experience, at the Charity Hospital in which approximately 20 000 spinal anesthetics have been administered using procaine, tetracaine, and dibucaine the writer has noted no major neurologic complication Experience of others who have used spinal anesthesia to any extent coincides with that of the writer In institutions where three or four paraplegias have been reported in as small a series as five or six hundred spinal anesthetics it behooves the workers to critically review their technique, the drugs and other technical factors which might be responsible for the complication

The etiology of the cauda equina syndrome is not known Contrary to current impression the incidence is no higher with the longer lasting, more potent drugs than with the short acting The incidence is no greater with tetracaine and dibucaine than with procaine In animals transient changes occur in the meninges and in the spinal cord when the currently employed drugs

in concentrations ordinarily advocated for clinical anesthesia in man are used These changes last several days unless the dose ordinarily used for spinal anesthesia is exceeded, in which case they persist for a longer time Attempts to reproduce the cauda equina syndrome in animals have been successful only when concentrated solutions have been used Some feel that the concentration rather than the total dosage is the most important factor Data in support of this contention is not adequate A number of neurologists feel that pre existing neurologic disease such as cord tumor, degenerations of the cord, myelitis, etc, are aggravated by lumbar puncture and the symp toms of cauda equina syndrome are abruptly precipitated Trauma to the cord by the spinal needle has been incriminated This is a possibility when the lumbar puncture is performed above the second lumbar vertebrae In less than 10% of patients, the cord extends below the second lumbar but in the majority it ends between first and second lumbar vertebrae The caustic solutions used for sterilizing ampules of drugs may pass into the ampule through microscopic cracks Ampules sterilized with alcohol or formalin should be submerged completely, the solution should be tinted with a brightly colored dye and each ampule should be inspected before the drug is used Detergents and other materials used for cleaning needles have been in criminated and have been known to cause neurologic changes Chemicals other than the local anesthetic drug have been injected Ampules containing mercurial diuretics have been mistaken for those of local anesthetic drugs and were inadvertently injected intrathecally with serious consequences The possibility that precipitation of the local anesthetic drug as it comes into contact with the alkaline spinal fluid may cause damage to the cord has been suggested The precipitate resting upon the cord and nerve roots could cause damage to the nervous tissue Allergy is always mentioned in a discussion of any reaction involving drugs It is possible, but not probable that allergy plays a role in causing the syndrome The etiology of this crippling syndrome remains to be discovered The possibility of its occurrence is feared by both surgeons and anesthetists It is the one factor which is limiting the general acceptance of spinal anesthesia

### Meningeal Infections

Meningeal inflammation results from contamination of the epidural and subarachnoid space during induction of anesthesia or from unrecognized pre existing infection which manifests itself fully after the block In the latter case, spinal anesthesia was merely incidental to the infection The meningococcus is the most common organism found When due to contamina tion from errors in technique, the staphylococcus is the most common causa tive organism found After an incubation period of several days, the patient develops the classical signs of meningitis The diagnosis is easily made by examination of the spinal fluid Epithelium from the skin and connective

tissue from the interspinous ligaments has been found in spinal fluid, pre sumably having been pushed into the subarachnoid space by the needle Thorough cleansing of the skin is important Infection may result from con taminated glucose or local anesthetic solutions, or needles, gloves or drapes which have not been properly sterilized

Paraplegias, palsies, and meningeal infections have also been reported after general anesthesia Pre existing neurologic disease such as tabes, combined degeneration and multiple sclerosis may be the causative factor Thrombosis of the spinal artery may occur postoperatively incidental to the operation and not related to anesthesia Neurologic sequelae are more frequent after the use of the continuous or serial spinal anesthesia, than the single injection technique

BACKACHE

Backache is not a neurologic complication However it is one which is occasionally encountered after spinal anesthesia and considered along with neurologic complications The etiology is difficult to determine It is possible to advance the needle too far and traumatize a disk Herniation then occurs Trauma to the interspinous ligament may occur The periosteum may be traumatized after repeated attempts at lumbar puncture and may cause the backache More likely, the backache is not related to the spinal anesthetic, but is due to pre existing orthopedic disturbances Relaxation of skeletal structures from anesthesia while on the operating table or being confined to bed in the postoperative period may have some bearing upon its appearance postoperatively Frequently pre existing backache is aggravated by loss of muscle tone relaxation of the ligaments, and other factors Backache, of course, is frequently seen in many surgical patients irrespective of the type of anesthesia

## Epidural Anesthesia

Epidural anesthesia *is induced by injecting a local anesthetic drug into* the epidural space The site of injection is usually in the lumbar area How ever the thoracic area or even the cervical has been used in the technique known as *segmental epidural* block An observation tube with a capillary lumen containing saline is attached to a lumber puncture needle A negative pressure indicates the tube is in the epidural space (Fig 18) The technique of inducing an epidural block is rather meticulous since shifting the needle and advancing it an additional millimeter or so may cause the drug to pass into the subarachnoid space instead of the epidural The concentration of drug employed is approximately ten times greater than that used for sub arachnoid block An error in technique may result in a total spinal block which, of course is not only undesirable but hazardous Unless one is adept in inducing epidural block, the technique is best reserved for "experts"

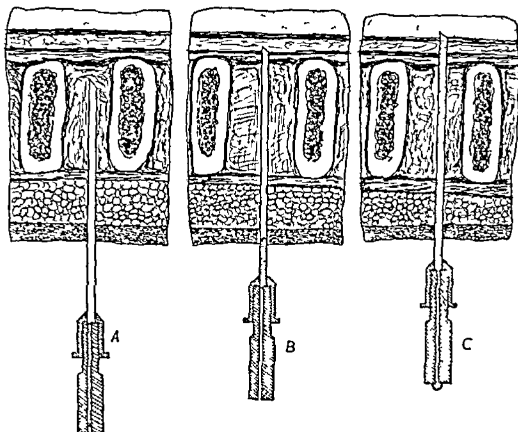



FIG 18 Method of performing lumbar epidural block (A) Needle fitted with glass adapter The lumen of the adapter which has an extremely fine bore is filled with procaine solution or saline (B) The needle is shown with the bevel in the epidural space (C) Improper placement of needle is shown The needle is in the subarachnoid space The flow of spinal fluid indicates the needle has been advanced too far and the technique will therefore have to be abandoned

There is a widely accepted misconception that hypotension and other physiologic changes characteristic of spinal anesthesia do not occur during epidural block In a successful block sensory, motor and autonomic blockades result The hypotension and other derangements typical of spinal anesthesia appear and are managed in exactly the same manner The mechanisms causing them are presumably the same

## Caudal Block

Caudal block is a modification of epidural block The drug is introduced into the caudal canal which is merely a continuation of the epidural space into the sacrum (Fig 19) It is possible to force the solution from the sacral hiatus to the foramen magnum by using volumes of solutions of 50 cc or more Under these circumstances circulatory changes characteristic of spinal anesthesia also occur In the ordinary caudal block the changes are not striking From the standpoint of circulatory changes caudal block is safer than spinal anesthesia but is not entirely free from hazard The same difficulties

and objections of spinal anesthesia may be encountered, particularly in poor risk patients Other factors to be considered are toxic reactions from the comparatively large amount of drug used, from rapid absorption, or from accidental intravenous injection Establishment of anesthesia requires 15 or 20 minutes In addition induction of the block from a technical standpoint is more time consuming than a low spinal or saddle block A catheter may be introduced into the caudal and the dose is repeated a number of times The technique is then called *continuous caudal block*, or *serial caudal block* Headache following caudal block is uncommon The cauda equina syndrome may occur after caudal block but is extremely rare

## Infiltration and Nerve Blocks

Local anesthesia by infiltration or nerve block causes no significant disturbances other than those due to systemic absorption of the drug or to distension of tissue by the solution, particularly in painful areas Vasodilatation occurs distal to the site of application of the drug in the nerve block Edema, the possibility of reduced wound healing, and distortion of tissues preclude the use of infiltration techniques in certain cases

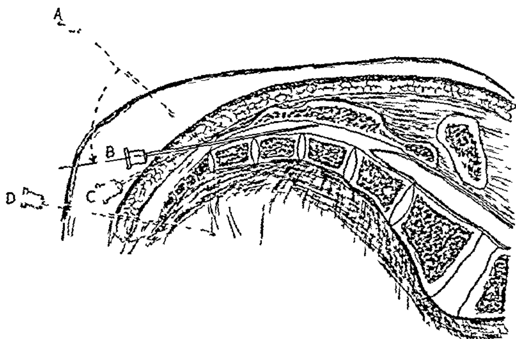



FIG 19 Cross section of the sacrum showing induction of a caudal block (A) Position of needle while contacting the sacral coccygeal membrane in attempting to penetrate the canal (B) Position after the needle has pierced the membrane and is entering the caudal canal Note that the needle lies in a plane almost parallel to the surface of the sacrum (C) Incorrect placement of the needle when the hiatus is inaccessible or missed The needle lies on the surface of the sacrum (D) The needle is introduced into the pelvis This occurs if the tip of the coccyx is mistaken for the sacro-coccygeal joint The dural sac usually ends at the level of the second sacral foramina Note that the space in the caudal canal is continuous with the peridural space Solutions introduced into this space may extend as high as the foramen magnum

Local anesthesia is selected in the poorest risk patient because other methods of anesthesia are considered too hazardous This idea, which is deep rooted in the minds of most physicians, is not necessarily correct Many times local anesthesia may be a poor choice for these patients The trauma, blood loss, reflex changes, and other deleterious effects of surgery are no more minimized by local than other forms of anesthesia Too often local anesthesia is not satisfactory for obtaining complete pain relief, and the surgeon is handicapped in performing the operation properly Also many patients are not psychically suited to undergo surgery under local anesthesia

## REFERENCES


Abajian J Peridural segmental anesthesia *Anesthesiology 4* 372–382 1943

Adriani J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 86

Adriani J *The Techniques and Procedures of Anesthesia* Springfield Thomas 1947 p 200

Adriani J *The Chemistry of Anesthesia* Springfield Thomas 1946 p 444

Adriani J and Roman D A Saddle block anesthesia *Am J Surg 71* 12, 1946

Arrowood J G Sarnoff S J Differential spinal block *Anesthesiology 9* 614 1948

Bonica J J Regional anesthesia with tetracaine *Anesthesiology 11* 737–744 1950

Crossman L W Allen I M *et al* Refrigeration anesthesia *Anesth & Analg 21* 241 1942

Davis L *et al* Pathology following spinal anesthesia *Am J Surg 97* 1781 1931

Greene O G Lumbar puncture headaches *Anesthesiology 11* 702–708 1950

Graubard D and Peterson M *Intravenous Procaine* Springfield Thomas 1950

Haraldson S Headache after spinal anesthesia experiments with a new spinal needle *Anesthesiology 12* 321 327 1951

Judovich B D Bates W and Bishop K Intraspinal ammonium salts for the intractable pain of malignancy *Anesthesiology 5* 341 1944

Kaplan M S and Arrowood J G Prevention of headache following spinal anesthesia the use of epidural saline *Anesthesiology 13* 103–110 1952

Labat G *Regional Anesthesia* 1st Ed Philadelphia Saunders 1927

McCuskey C I Regional anesthesia for office procedures *California Med 76* 213 1953

Odom C B Epidural anesthesia *Am J Surg 34* 547 1936

Roman D A and Adriani J Nupercaine glucose for spinal anesthesia results of over 5000 clinical administrations *Anesthesiology 10* 270–279 1949

Schumacher L I and Eversole U H The techniques of spinal anesthesia *Anesthesiology 3* 630–643 1942

Smith H W Rovenstine E A Goldring W *et al* The effects of spinal anesthesia on the circulation in normal unoperated man with reference to autonomy of the arterioles and especially those of the renal circulation *J Clin Investigation 18* 319 1939

# XII

# MUSCLE RELAXANTS

## THE INTRODUCTION OF CURARE INTO ANESTHESIA

The muscle relaxants were introduced as adjuncts to anesthesia in 1943 They are now widely used for major surgery Originally, curare was the sole muscle relaxant available Claude Bernard, the physiologist, described its pharmacologic action in 1840 Before 1936 specimens of curare were of unknown composition and of doubtful purity The drug remained a pharmacological curiosity for many years Richard Gill, an American explorer, was instrumental in locating and bringing to the United States from South America the authenticated, botanical specimen which contains the drug Curare is an extract of the stems, bark, and leaves of the plant, chondrodendron tomentosum The active principle in curare is the alkaloid, tubocurarine Preparations of curare heretofore contained ingredients derived from other plants related to curare, which were harvested along with the curare These foreign substances were responsible for the undesirable reactions such as bronchial constriction, circulatory collapse, respiratory failure, and convulsions

## MODE OF ACTION

Since the revival of curare and the isolation of its active principle, other muscle relaxing drugs have been introduced With few exceptions these are synthetic substances The ultimate result is the same for all substances muscle relaxation Each has advantages and disadvantages It is simpler to study the muscle relaxants in groups based upon similarity of pharmacologic action, rather than as individual compounds From a pharmacologic standpoint muscle relaxants may be placed into four groups In the first group are drugs which *act centrally* to block passage of motor impulses Mephenesin (Tolserol) acts at the internuncial neurons in the spinal cord and possibly at the higher centers (thalamus) Motor activity is inhibited centrally rather than peripherally The second group includes drugs which *prevent acetyl choline from acting* at the neuromuscular junction Curare acts in this manner The third group is composed of drugs which cause *persistent depolarization* of the membrane at the neuromuscular junction The fourth group includes drugs which *inhibit muscle fibers* directly Quinine acts by prolonging the refractory period and inhibiting contractility of striated muscle

The important drugs, as far as anesthesia is concerned, are those which prevent acetyl choline from acting and those which induce sustained depolarization at the membrane The group which prevents acetyl choline from

acting includes curare, its alkaloid tubocurarine, synthetic derivatives of tubocurarine, the erythrina alkaloids, gallamine and benzoquinonium (mytolon) The methyl ether of tubocurarine (metubine or mecostrin) is prepared from tubocurarine It possesses an action qualitatively similar to tubocurarine, but quantitatively different The drugs causing sustained depolarization will be discussed later

## PHYSIOLOGY OF NEUROMUSCULAR TRANSMISSION

In order to understand how muscle relaxants act, it is important to know the normal physiologic action at somatic motor nerve endings As the impulse or excitation wave passes to a nerve ending, acetyl choline is liberated The acetyl choline passes through the subneural space to the junctional membrane At rest the membrane is in an electrical state referred to as polarized The acetyl choline alters the electrical charges on the membrane and causes it to become depolarized Depolarization initiates contraction of the muscle fibers As soon as the stimulus resulting from the depolarization recedes, the muscle fiber relaxes to its resting state and remains relaxed until the membrane becomes repolarized It is once again capable of responding to a succeeding impulse If the membrane is not repolarized, succeeding impulses are without effect and the muscle remains relaxed If acetyl choline accumulates at the neuromuscular membrane, depolarization persists and the muscle remains relaxed In order for a muscle fiber to have tone and to contract, the acetyl choline must be quickly removed after a stimulus so that the membrane will be ready for the next nerve impulse This is accomplished by the enzyme, cholinesterase, which hydrolyzes the ester into acetic acid and choline It is estimated that the hydrolysis occurs within 1/1000 of a second The membrane then regains its polarity and is ready to receive the next impulse Obviously, then, an excess of acetyl choline can cause persistent depolarization and paralysis of a muscle fiber Tubocurarine and its derivatives and other substances acting similarly are fixed in some manner at the neuromuscular membrane and prevent the depolarizing action of acetyl choline The membrane then remains polarized and the muscle fiber is unable to contract because the acetyl choline, even though it is liberated after each nerve impulse, and reaches the muscle fiber, is unable to act Two newly introduced synthetic substances which are believed to act in the same manner are gallamine (flaxedil) and benzoquinonium (mytolon)

## REVERSAL OF CURARE EFFECTS

The blockade caused by curare and curare like drugs may be reversed in one of two ways (1) by using a substance which inhibits cholinesterase Acetyl choline then accumulates in sufficient amounts to overcome the so called blockade or barrier, and (2) by using a drug which displaces curare or is combined with it Physostigmine and neostigmine are two drugs used to

inhibit cholinesterase and prevent *the hydrolysis of acetyl choline* A number of esters derived from phosphoric acid such as DI P (di isopropyl fluoro phosphate) and HEP (hexaethylpyrophosphate) also destroy or inhibit the enzyme These are not used in anesthesiology however Theoretically, cho linesterase inhibitors should reverse the action of curare and curare like drugs In actual practice the results are disappointing In cases of over curarization, they actually enhance the effect rather than overcome it

The *most satisfactory antagonist* is a substance related to prostigmine known as edrophonium (Tensilon), (phenyl trimethyl ammonium hydrox ide) Presumably *it acts by combining with the relaxant and removing it* from the site of action The acetyl choline is then free to initiate the con traction in a normal fashion Edrophonium, eserine, and neostigmine also cause a sustained effect at the post ganglionic parasympathetic nerve end ings The acetyl choline liberated there is not hydrolyzed rapidly either Symptoms of parasympathetic stimulation occur concomitantly with the anti curare effect Slowing of the pulse rate, contraction of the bowel, saliva tion, secretion of mucus, and other undesirable side actions are common Anti cholinergic drugs such as atropine, scopolamine, and hyoscyamine pre *vent these reactions* The usual *dose of edrophonium is from 5 to 10 mgms* depending upon the degree of over curarization The drug is combined with 1/100 to 1/150 gr of atropine or an equivalent dose of another anti cho linergic drug Edrophonium is short acting After 5 to 10 minutes, its effects pass off If an excess of muscle relaxant is still present in the body, respiratory failure may once again ensue Patients should not be left unat tended after the drug has been used until it is certain that the reversal is sustained It may be necessary to repeat a dose of edrophonium a second time if signs of curarization reappear

## DRUGS CAUSING SUSTAINED DEPOLARIZATION

*Muscle relaxants which cause persistent depolarization are decamethonium* and succinyl choline They act as though acetyl choline were present in excess *at the junctional membranes* The membrane remains depolarized and the impulses are without effect The muscle fibers remain atonic Any drug which has an acetyl choline like action and causes sustained depolarization at the junctional membrane of skeletal muscle has this effect Fasciculations or generalized convulsive movements follow injection of these drugs These usually persist for 20 to 30 seconds and then relaxation ensues They may not appear if the drug is administered slowly Decamethonium (syncurine) is the best known of this type drug A new preparation which offers promise of being clinically useful is succinyl choline (anectine) It appears to be safer than the muscle relaxants heretofore studied, largely due *to the mode of* detoxification

## DETOXIFICATION OF MUSCLE RELAXANTS

Succinyl choline is hydrolized to succinic acid and choline by the aid of cholinesterase This hydrolysis occurs rapidly but compared to the hydrolysis of acetyl choline, it is slow Within three minutes most of a dose is hydrolyzed, and muscle tone returns Most muscle relaxing agents are eliminated unchanged by the kidney, or are partly destroyed by the liver and partly eliminated unchanged into the urine Duration of action depends to a great extent upon the rate of elimination Some act longer than others When cholinesterase levels are below normal the action of succinyl choline is prolonged Levels may be low in liver diseases, starvation and after chronic diseases Cholinesterase inhibitors such as edrophonium, neostigmine, and eserine retard the hydrolysis and cause a sustained effect Unlike the effect they have on curare, they do not antagonize the action of succinyl choline or decamethonium In fact they enhance it The by products of the hydrolysis, succinic acid and choline, are naturally occurring body constituents The advantages in having the detoxification products of a drug not be biologically foreign to the body are obvious

## EFFECTS ON RESPIRATION

In many instances when muscle relaxants are used as adjuncts to anesthesia, the respiratory pattern is disturbed and does not return to normal for quite some time The respiratory paralysis which follows the administration of muscle relaxants is due by and large to the peripheral effect on the muscles of respiration There is also some evidence that the respiratory depression may be of central origin In curarized and apneic animals, stimulation of the phrenic nerves causes contraction of the diaphram This suggests that the peripheral action has disappeared and that the apnea is due to a direct depression of the respiratory center Sustained apneas due to this *presumed central effect are uncommon, however this must be borne in mind* as a possible occurrence As a rule when succinyl choline is used, as soon as the paresis disappears, the respiratory pattern is restored to normal Instances of sustained apnea are more frequent when other muscle relaxants are used

## CONTROLLABILITY

Another reason why succinyl choline is preferred to other relaxants is that the blockade may be interrupted at will When a sustained blockade is desired, the drug is administered by a continuous intravenous drip Ordinarily the single injection method is suitable for brief periods of relaxation Twenty mgm in a single dose for adults of average size causes a momentary apnea lasting 50 or 60 seconds followed by a gradual return of respiration to normal (within five minutes or less) No suitable antagonist is available for succinyl choline and decamethonium The doses ordinarily used for muscle relaxation

do not appear to affect the central nervous system There is neither stimulation nor depression

## POTENTIATION BY ANESTHETICS

Certain anesthetics have a curare-like action which either enhances the effects of muscle relaxants or causes an additive effect Ether, in particular, potentiates curare, tubocurarine, and similar acting drugs Decamethonium and succinyl choline are not potentated by ether or other central nervous system depressants Cyclopropane, ethylene, and nitrous oxide have little or no potentiating effect on curare and its derivatives

## RELATIONSHIP OF CHEMICAL STRUCTURE TO POTENCY

The muscle relaxants are bases which contain two pentavalent nitrogen atoms These nitrogen atoms are spaced 15 angstrom units apart (an angstrom unit is 1/10,000,000 of a millimeter) Placement of the nitrogen atoms at a greater distance lessens their curare like action When brought closer together the curare like action likewise is diminished Decamethonium is also called C10 because the nitrogen atoms are separated by a straight chain of 10 carbon atoms Shortening the chain to 6 carbon atoms results in hexamethonium (C6) The muscle relaxing effects disappear and a ganglionic blocking effect appears Tubocurarine, gallamine, benzoquinonium, succinyl choline, and other relaxants all have two nitrogen atoms spaced 15 angstrom units apart In the case of tubocurarine, complex cyclic nuclei separate them In others, various chemical groups are interposed between the nitrogen atoms Inasmuch as the muscle relaxants are basic, they form salts with acids They are incompatible when combined with alkaline substances If mixed with solutions of sodium salts of barbiturates, precipitation occurs, unless the solution is very dilute

## EFFECTS ON THE CENTRAL NERVOUS SYSTEM

The muscle relaxants are not anesthetic, analgesic, or hypnotic Surgery may be performed on a curarized patient without any struggling because the subject is incapable of voluntary movement and is unable to resist The central nervous system remains active, however, and the subject feels pain and remembers the experience In present day practice it is customary to combine the muscle relaxants with basal narcotics Usually thiopental, thiosecobarbital, or evipal are used The basal narcotic supplies the hypnotic and amnesic effect not possessed by the muscle relaxant However, neither drug blocks painful stimuli A third substance must be added for analgesia For this reason it is common practice to combine nitrous oxide which supplies analgesia, thiopental which supplies basal narcosis, and a muscle relaxant which supplies the relaxation Relaxation is not obtained with safety using nitrous oxide or thiopental alone The use of the triple combination

permits a decrease in the amount of each drug and increases the margin of safety It must be remembered when using combinations of drugs that the hazards of each drug are additive

## EFFECTS ON THE AUTONOMIC NERVOUS SYSTEM

Muscle relaxants possess other actions of interest Doses greater than the curarizing dose causes block at the autonomic ganglia The effects of doses ordinarily used for anesthesia are of little clinical significance Some of the newer synthetic substances manifest vagal stimulating or depressant effects Curare, tubocurarine, and the methyl ether of tubocurarine have a histamine like action and have on occasions caused intense bronchospasm This must be borne in mind during bronchoscopy, laryngoscopy, and thoracic surgery Bronchial constriction is best relieved by the use of substances such as aminophylline which act directly on the bronchial musculature

## EFFECTS ON CIRCULATION

In the light of our present knowledge, the muscle relaxants have no appreciable effect upon the heart Deaths due to cardiac failure immediately or shortly after administration of the drug are unknown Many fatalities are due to asphyxia resulting from the respiratory failure If adequate ventilation is maintained by artificial respiration until the curare effects disappear, respiration will resume and no difficulties are encountered There is, however, a dose which is lethal even though ventilation is adequately maintained In dogs the fatal dose of curare is approximately five times that which causes cessation of ventilatory efforts by complete curarization Apparently these drugs possess an inherent toxicity Fatalities are more frequent than is believed when muscle relaxants are used as adjuncts to anesthesia The usual sequence of events in these fatalities is that respiration fails after the drug is administered As the effects recede, the respiratory exchange returns, but not to the normal pattern There is then a gradual deterioration of the circulation and the patient dies from circulatory failure Prolonged sustained curarization causes hemoconcentration and a shock like state in animals In man the blood pressure is often decreased due to the muscle relaxation, which in turn causes a reduction in the venous return to the heart In general, subjects in good physical condition suffer no adverse effects from the muscle relaxants as far as the cardiovascular system is concerned

## METABOLIC EFFECTS

Liver function renal function, acid base balance, blood sugar, nonprotein nitrogen, and carbohydrate metabolism are not disturbed by the muscle relaxants Blood morphology, bleeding time, and clotting time are not affected Glandular secretions are not inhibited by muscle relaxants Smooth muscle is not relaxed by curare or its allies The drugs are not suitable for

operative obstetrics because they have no effect upon the uterus The muscle relaxants pass through the placenta to the fetus

## USES

The muscle relaxants are used only when muscle relaxation is required This statement may appear strange However, some anesthetists use muscle relaxants routinely whether they are indicated or not Their use for superficial operations such as craniotomy, mammectomy, plastic operations, obstetrics and other instances in which muscle relaxation is not required or can be obtained without them is indicative of lack of thought and judgement The muscle relaxants facilitate relaxation of the jaw and neck muscles to accomplish successful intubation Abdominal surgery may be performed with much lighter inhalation anesthesia than ordinarily would be required without them Some anesthetists employ muscle relaxants to cause respiratory paralysis during thoracic surgery Respiration is then maintained artificially either by a mechanical device or by intermittent insufflation of the bag of the anesthetic apparatus manually Certain endoscopic procedures such as bronchoscopy, laryngoscopy, and esophagoscopy are facilitated by use of muscle relaxants A combination of the relaxant, a basal narcotic, and topical anesthesia is used

### REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 92

ALEHMANN A Succinyl choline chloride in liver damage *Lancet* *2* 123 1953

COLE F C A near fatal dose with curare with some observations on the pathology produced by large doses *Anesthesiology* *7* 190–197 1946

GRIFFITH H R and JOHNSON G E The use of curare in general anesthesia *Anesthesiology* *3* 418–421 1942

GRIFFITH R H STEPHEN R C *et al* Myanesin as a muscle relaxant *Anesthesiology*, *10* 61 1949

HUNTER A R The anti curare agents *Brit M J* *1* 640 1953

ROBBINS B H and LUNDY J S Curare and curare like compounds *Anesthesiology* *8* 348–357 1947

UNNA H R PELIKAN E W and MCFARLANE M S *et al* Evaluation of curarizing agents in man *J A M A* *144* 448 1950

XIII

# ANALEPTICS AND ANTI-NARCOTIC DRUGS

## NATURE OF CENTRAL NERVOUS SYSTEM DEPRESSION

The medullary centers are the last of the intracranial centers to become depressed when central nervous system depressants are administered The respiratory center is one of the first of the medullary centers to become inactive and respiratory failure ensues The intracellular metabolic processes are disrupted by depressant drugs Unless irreversible changes are instituted by an excess of the drug, cellular activity is usually restored to normal by removing the drug In the case of the volatile central nervous system depressants, removal of the excess is accomplished by artificial respiration A pressure gradient is established from the cells, to the blood, to the alveolar air, and to the outside atmosphere The problem is not as simple with nonvolatile drugs

Two schools of thought exist on the management of over dosage of central nervous system depressants One group feels that if the circulatory system is supported by fluids and stimulants, and if ventilation is adequately maintained by artificial respiration, in due time the drug will be eliminated and recovery will follow Others feel that therapy is indicated with drugs which reverses narcosis by stimulating depressed centers

## NATURE OF ANALEPTICS

Drugs used to reverse narcosis are called analeptics The word analeptic, which is of Greek derivation, means restorative An analeptic is usually defined as being a central nervous system stimulant suitable as a therapeutic substance to overcome depression of that system Not all central nervous system stimulants are satisfactory as analeptics Procaine, for instance, stimulates the central nervous system but is useless as an analeptic Strychnine is a stimulant also but exerts its effect primarily on the spinal cord where its action is of no benefit The most useful stimulants for overcoming narcosis exert their primary action on the medullary centers Some central nervous system stimulants atropine for example, appear to act in a uniform manner on the entire central nervous system Others exert their action primarily on the cerebrum The medulla is stimulated only when large doses of this type are given Caffeine in small doses stimulates the cortex Large doses are required to stimulate the medullary centers Strychnine stimulates from below upward, the cord first, then the medulla, and then the higher centers Drugs which stimulate the central nervous system depress it as a rule

when given in excess The most useful stimulating drugs from a clinical standpoint act primarily on the respiratory centers

## TYPES OF ANALEPTICS

Analeptics may be placed into five groups according to their mode of action The first group includes drugs whose stimulating action is primarily on the vital medullary centers Picrotoxin, nikethamide, and pentamethylene tetrazole (metrazol) act primarily *on the medullary centers* Larger doses stimulate the cord or the structures above the medulla

The second group includes drugs acting reflexly to stimulate vital centers Most important are substances acting on the carotid body, which in turn reflexly stimulate the respiratory center Lobeline, various cyanides, and nicotine act on chemoreceptors They probably act by inhibiting the respiratory enzymes in the cells of the receptors The cells respond in the same manner as they would if the oxygen tension were reduced In the face of anoxemia, obviously, they are of no avail Sensory nerve stimulants such as ammonia, subcutaneous ether, and camphor in oil reflexly stimulate the central nervous system in mild states of depression In severe states of depression they are of no value Physical agents are not drugs but they should be mentioned in this discussion because they are still used by some clinicians Submersion in cold water, slapping the skin, pressure on nerves, such as the supraorbital, and dilatation of sphincters reflexly stimulate the nervous system when it is mildly depressed A severely depressed nervous system rarely responds to such stimuli

The third group includes drugs which improve the cerebral circulation and restore the activity of vital centers by overcoming the medullary anemia accompanying circulatory failure They usually cause a hypertension by inducing vasoconstriction and improving cardiac output Such drugs are of little value in overcoming the effects of central nervous depressants They are useful, *however, in overcoming the depression due to "neurogenic shock"* such as the type encountered in spinal anesthesia

Drugs in the fourth group stimulate both the vital centers and the cardiovascular system By this dual action, they stimulate the centers and raise the blood pressure to improve the medullary blood flow Overlapping exists between drugs in this and the first group The cardiovascular effects of drugs in the first group are not of remarkable significance Benzedrine and desoxyephedrine are examples of drugs which possess a dual action

The fifth group includes drugs which modify or reactivate cellular metabolism It is *believed that depressant drugs inhibit utilization* of oxygen by the cells by interfering with the action of respiratory enzymes The metabolites customarily utilized by the cells are not oxidized because the enzyme system is in some manner inactivated by the depressant drug However, the administration of a metabolite which the cell can use but does

not ordinarily use and which is catalized by an enzyme system not influenced by the narcotic, causes oxidation to be resumed The substitution of succinic acid as the metabolite when the oxidation of glucose has been interrupted is based upon this premise Oxidation then proceeds and recovery occurs In vitro and in some animal studies, sodium succinate had been effective in reversing narcosis, but the results clinically in man have been disappointing

## MODE OF ACTION OF ANALEPTICS

The mode of action of analeptics is not known Some of the suggestions made are as follows (1) The drug may neutralize or inactivate the narcotic This is possible but not probable (2) The drug may decrease the concentration of the narcotic in the cell This likewise is possible but not probable (3) *The analeptic may displace the narcotic from combination with the respiratory enzymes*, notably the dehydrogenases or may act as coenzymes in the oxidation reduction systems In this way it restores activity to the respiratory enzymes This is a strong possibility Analeptics usually do not stimulate respiration in the absence of narcotics Picrotoxin, for instance, may produce convulsions without manifestations of respiratory stimulation On the other hand in animals narcotized with barbiturates, less than the convulsive doses *of picrotoxin causes respiratory stimulation Analeptics do not overcome* depression of the nervous system due to anoxia or asphyxia

## SIDE ACTIONS CAUSED BY ANALEPTICS

Besides stimulating the respiratory center, analeptics may stimulate the other medullary centers, particularly the vasomotor and the vomiting centers Elevations in blood pressure and nausea and vomiting may occur after their administration *Emphasis is often placed on the effects of analeptics upon* the heart Little if any increase in cardiac output is caused by most analeptics When an increase does occur it is usually not of clinical significance with the currently used drugs When analeptics are used to excess, the stimulation may be widespread and convulsions may follow Convulsions are more likely to occur in mild depressions There is a latent period from the moment the drug is injected until the stimulation manifests itself In severe depressions, *the stimulating action is fleeting and short lived The stimulation recedes and* the depression then reappears

## OBJECTIONS TO THE USE OF ANALEPTICS

Many anesthesiologists are violently opposed to the use of analeptics One objection they have is that such drugs neither accelerate detoxification nor facilitate elimination of the depressant drug The body is then confronted with the problem of eliminating two drugs instead of one A second objection offered is that a depression may follow stimulation and that this is superimposed upon the depression caused by the narcotic This is true when an

excess is given and convulsions occur Depression invariably follows convulsions precipitated by analeptics A third objection is that analeptics increase the oxygen consumption of cells already depressed by co existing anoxia Stimulation increases metabolism Any increase in metabolism increases oxygen consumption which of course is undesirable in the face of an already existing anoxia A fourth objection is that side actions, such as nausea, vomiting tremors, twitchings, elevation in blood pressure, etc , follow the use of analeptics A fifth objection is that convulsions may follow inadvertent administration to a patient mistakenly assumed to be overdepressed

## CURRENTLY USED ANALEPTICS

The more important analeptic and anti narcotic substances in present day use are metrazole, nikethamide, picrotoxin and N allyl nor morphine (Nalline) Metrazole (pentamethylene tetrazole), stated as being related to camphor, is a nitrogen containing heterocyclic structure It is a water soluble stable substance which is effective intravenously, intramuscularly, and orally It stimulates the medullary centers primarily A brief latent period of less than one minute precedes stimulation When administered intravenously a peak effect is obtained within 2 to 3 minutes, which is sustained for a period of several minutes more (Fig 20) The stimulation then recedes sometimes abruptly sometimes gradually, necessitating a repetition of the dose

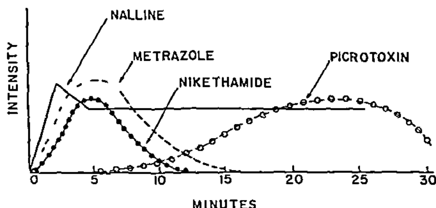



Fig 20 The relationship of onset and intensity of action to time manifested by metrazole nikethamide picrotoxin and N allyl nor morphine when used as analeptics during narcosis Note that the peak effect is reached within several minutes when metrazole is used Minute volume exchange is the criterion used to designate intensity of stimulation A latent period of 30 or more seconds precedes the onset of stimulation There is a gradual recession of respiratory activity after three or four minutes with a return to the pre injection state The latent period with nikethamide is somewhat longer the peak of action is not quite as intense and the duration of action is briefer compared to metrazole Picrotoxin manifests a long latent period with a gradual rise in intensity to a plateau which may be sustained as long as 25 or 30 minutes The intensity is greatest with the substance. The response depicted by these three drugs is by the intravenous route in a subject narcotized with barbiturate The N allyl nor morphine is used to reverse over dosage from morphine Note that the effect is sustained in contradistinction to the other analeptics

There is no remarkable effect upon the normal respiratory center until convulsions appear, at which time, of course, the cortex and midbrain are being stimulated Large doses also stimulate the vasomotor centers It is suitable for circulatory collapse of central origin, but not for that of peripheral origin or that due to loss of fluid The vomiting center is stimulated Nausea, vomiting and retching may occur during stimulation and afterward The drug is rapidly eliminated A convulsive dose is detoxified by the liver in less than an hour The spinal cord is stimulated by large doses Hyperirritability from strychnine and other cord stimulants is enhanced by metrazol The drug is absorbed from the stomach There is no clinically significant stimulating effect on the myocardium or conductive tissues, nor is there any appreciable dilatation of the coronary vessels A transient generalized vasodilatation occurs which may cause a momentary hypotension following intravenous injection

*Nikethamide* (coramine) is the diethylamide of nicotinic acid The respiratory center is stimulated reflexly via the sino aortic bodies There is also some direct stimulation of the medulla itself Like metrazol, it acts effectively only in the presence of depression due to drugs Large doses stimulate the cortex and cause convulsions This stimulation is then followed by respiratory depression and coma There is no significant clinical effect upon the heart Large doses may elevate the blood pressure due to reversal of depression of the vasomotor center The drug is rapidly inactivated presumably by the liver A latent period with a gradual build up to a peak effect like that of metrazol is also characteristic of nikethamide The intensity and the peak effect are not quite as pronounced, nor is its duration as long, however (Fig 20)

*Picrotoxin* is a non nitrogen containing substance often referred to as an amaroid It is composed of equi molecular portions of two substances known as picrotin and picrotoxinin The latter is a convulsant Picrotoxin is a biological product obtained from the berries of Cocculus Indicus, a plant indigenous to India In normal subjects, subconvulsive doses have no effect In patients who are depressed from hypnotics, particularly the barbiturates, the same subconvulsive dose causes stimulation of respiration Emesis may occur following its use Like metrazol and nikethamide, picrotoxin has a latent period also, but it is considerably longer—ten to fifteen minutes at times A plateau is gradually reached which is sustained for as long as thirty minutes (Fig 20) It is the most useful of the analeptics in the management of barbiturate overdosage, particularly when dealing with long, intermediate and short acting barbiturates

*N allyl nor-morphine* or *Nalline* is an anti narcotic This substance is prepared from morphine by substituting the methyl group on the nitrogen atom with an allyl group It has recently been introduced It effectively reverses the action of morphine and related alkaloids Its latent period

is brief Within one minute the respiratory stimulation is apparent Respiratory depression due to narcotics is reversed Once the reversal has occurred, the action is sustained It differs in this respect from metrazol, nikethamide, and picrotoxin The drug is also suitable for antagonizing respiratory depression due to synthetic narcotics such as methadon, meperidine, methyl morphinan, and nisentil Depression due to dihydromorphinone (dilaudid), heroin, metapon, dicodid, and codeine are also reversed It is ineffective in overcoming depression due to the volatile anesthetics and the non volatile drugs not classed as narcotics (chloral, paraldehyde, and the barbiturates) Its mode of action is not understood at present Possibly it displaces the narcotic from the enzyme systems Chemically and pharmacologically related to N allyl nor morphine is N allyl morphinan which appears also to have promise as an antinarcotic

*Alpha Lobeline* is derived from Indian tobacco which contains three alkaloids, alpha lobeline, beta lobeline, and lobelidine The alpha lobeline is resolved from the mixture Its action is largely on the carotid body, acting in somewhat similar manner as cyanides and nikethamide It has little or no direct action on the respiratory center It causes a brief period of stimulation, a gasping type of respiration Large doses depress the heart Its action is brief and transient It possesses a latent period of approximately a minute Its usefulness is limited to initiation of the gasp in the new born Repeated doses may cause circulatory collapse and marked depression of the nervous system

*Benzedrine and Caffeine* are not clinically useful respiratory stimulants because they have little or no effect on the brain stem unless used in large doses They act principally upon the cerebral cortex They may be used in overcoming the drowsiness which is present in the recovery phase of depression from barbiturates and other non volatile drugs

*Sodium Succinate* is a soluble substance which has been used to attempt to reverse respiratory depression due to barbiturates It is assumed that it acts as a substrate which is oxidized by the aid of respiratory enzymes which are not inhibited by barbiturates Tissue respiration, therefore, is able to proceed Results in man to date have been disappointing and the substance is no longer used by most clinicians

*Carbon Dioxide* is sometimes classed as an analeptic A depressed respiratory center rarely responds to carbon dioxide If the center were capable of responding it would respond to that which accumulates in the blood during respiratory arrest and no additional gas would be necessary Its administration is not only useless but may be harmful A respiratory acidosis usually exists in these circumstances and further addition may have an adverse effect on the circulatory system Besides excess carbon dioxide affects cardiac rhythm and causes vasodilatation A hypotensive state may develop or be enhanced if one already exists

## REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield, Thomas, 1953, p 107

ADRIANI, J *The Techniques and Procedures of Anesthesia* Springfield, Thomas, 1947, p 337

ADRIANI, J and KERR M Clinical experiences in the use of nalline as an antagonist to morphine and narcotics in surgical patients *Surgery, 33* 731 1953

BARRETT, R K The analeptic effect of sodium succinate on barbiturate depression in man *Anesth & Analg, 109* 952 1937

DILLE J M Picrotoxin pharmacology and use *J Pharmacol & Exper Therap, 53* 295, 1935

ECKENHOFF, J E HOFFMAN G L, DRIPPS R D N Allyl Normorphine an antagonist to the opiates *Anesthesiology 13* 242–251, 1952

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York, Macmillan 1941 p 267

PICKRELL L L and RICHARDS R K Pentothal metrazole antagonism *Amer J Physiol, 84* 202 1928

SCHMIDT C F Carotid sinus reflexes to the respiratory center *A J Physiol, 10?* 94, 1942

TUCCI J H, BRAZIER, MARY A MILES, H W FINESINGER J E A study of pentothal sodium anesthesia and a critical investigation of the use of succinate as an antidote *Anesthesiology 10* 25–39 1949

# XIV

# VASOPRESSORS AND VASOCONSTRICTORS

## MODE OF ACTION

The terms vasoconstrictor, vasopressor, sympathomimetic and adrenergic drug are used interchangeably by most clinicians There is a difference be tween these terms however, although in certain instances it is slight Vaso pressor responses are caused in a number of ways (1) The drug acts by direct stimulation of the vasomotor center in the medulla Carbon dioxide is well known for its central stimulating action (2) The drug may act upon the autonomic ganglia and raise the blood pressure by direct stimulation Useful therapeutic agents acting in this manner are not available (3) The drug may act on the adrenergic nerve endings and stimulate the receptor substance Epinephrine and its allies act in this manner Such drugs are called adrenergic drugs (4) The drug may stimulate smooth muscle directly and cause arteriolar constriction Pituitary extract acts in this-manner Substances which act on the receptor organs of the autonomic nervous system are the most widely used and the most important vasopressors These substances stimulate adrenergic post ganglionic nerve fibers

## CHEMICAL NATURE

The majority of vasopressor drugs are amines of which several types exist The better known and most useful are aromatic amines Epinephrine, ephedrine, neosynephrine, benzedrine, arterenol, desoxyephedrine, and so on, all fall into this category They are composed of an aromatic nucleus to which is attached a chain of two or three carbon atoms A primary or secondary amino group is attached at the opposite end of this chain Some derivatives also have hydroxyl groups on the aromatic nucleus Epinephrine, for instance, has two hydroxyl groups, neosynephrine has one Some compounds, for example, cobeferin, desoxyephedrine, and ephedrine have a hydroxyl group on the carbon chain attached to the aromatic nucleus Some have hydroxyl groups on both the aromatic nucleus and the carbon side chain (epinephrine) Some compounds do not have any hydroxyl group on any part of the molecule Benzedrine and benzedrex do not The compounds possessing hydroxyl groups on the aromatic nucleus are easily oxidized and are therefore relatively unstable A second group of compounds which mani fest pressor activity have no aromatic nucleus In other words, they are aliphatic amines Oenethyl, tuamine, and octin are derivatives which fall into this category Oenethyl, for instance, is 2 methylamino heptane Octin has eight carbon atoms Aliphatic amines with pressor activity have long

chains, usually more than six carbon atoms A third group is composed of a heterocyclic nucleus, that is a ring containing nitrogen, and various side chains Others have a cyclic radical on an aliphatic group Privine and cyclopentamine (clopane) are so constituted Others have both aromatic and heterocyclic nuclei The number of substances manifesting some degree of pressor activity is so great that it is impossible to mention their chemistry or pharmacology in this discussion Only those of interest to anesthesiologists and surgeons are discussed

All amines whether primary, secondary, or tertiary are basic Aqueous solutions are alkaline They form salts with mineral and organic acids The bases are poorly soluble in water, but soluble in organic solvents and oils The salts are water soluble The stability varies Compounds containing hydroxyl groups are less stable than those which do not

## PHARMACOLOGY

In general these compounds are vasopressors, that is, they raise blood pressure They are vasoconstrictors and decrease the cross sectional area of the vacular bed They cause sympathetic stimulation in organs innervated by postganglionic, adrenergic fibers These derivatives are qualitatively similar, although quantitatively they may vary widely in their responses Some compounds act on the vascular bed of one organ causing a constriction, but have no effect or may even dilate the vessels of other vascular beds in other parts of the body Epinephrine constricts vessels in the skin and in the splanchnic areas, but dilates the vessels in the muscles and in the heart Others such as pituitrin cause generalized vasoconstriction No differentiation is made from one vascular bed to the other

The interest in vasoconstrictors and vasopressors in anesthesiology is threefold (1) they are used for vasoconstriction to prolong the action of local anesthetic drugs, (2) they are used as vasopressors to raise the blood pressure in hypotensive states, and (3) they are used as analeptics to stimulate the cerebral and medullary structures

Epinephrine is the best known, but the least useful of these amines as far as pressor effects during anesthesia is concerned In general, epinephrine is fleeting in its action, causing tremor and tachycardia, and is not a suitable pressor substance It increases cardiac irritability and causes a disturbance in rhythm In addition it may decrease peripheral resistance by dilating certain parts of the vascular system Arterenol or norephrinephrine is used to raise blood pressure in hypotensive states but must be administered by a continuous infusion because its action also is evanescent This substance causes a generalized vasoconstriction It is used successfully in hypotensive states which do not respond to fluids and other vasoconstrictors suitable for controlling hypotension The most useful vasopressor drugs from the standpoint of anesthesia are those having a prolonged sustained action Most

important in this category are ephedrine, desoxyephedrine, neosynephrine, vasoxyl, and oenethyl These substances administered intramuscularly or intravenously cause a sustained pressor effect Pituitrin *acts by stimulating* smooth muscle directly There is some evidence that it acts upon the capillaries also The chief objection to pituitrin and pitressin is that they cause the coronary vessels to constrict and induce myocardial ischemia Sympathomimetic drugs apparently do not have this effect As a matter of fact, evidence exists that they act in the reverse manner

## USE FOR HYPOTENSION

The success of vasopressors in overcoming hypotension depends upon the mechanism causing the fall in blood pressure Vasopressors are not suitable in hypotensive states due to a loss of fluid and reduction in blood volume Vasoconstriction is present or has been present for some time in these situations The hypotension indicates that mechanism has failed Additional attempts at vasoconstriction may hinder the situation rather than better it Vasopressors are suitable when hypotension is of nervous origin, that is, in "neurogenic shock" Hypotension of the type which occurs during spinal anesthesia, after traction on the mesenteries or after stimulation of the perineal areas, and so on may be overcome with vasopressors In situations in which the hypotension is due to fluid loss after fluid deficiency has been corrected, the cautious use of vasoconstrictors may be of benefit if the blood pressure is not at its pre hypotensive level Most vasopressors exhibit the phenomenon known as tachyphylaxis Successive doses of a drug have progressively less effect until a point is reached where the drug is no longer effective, or may even have the opposite effect After a third or fourth dose, the vasopressor response to ephedrine disappears or is slight (Fig 21)

## CHARACTERISTICS OF A SUITABLE VASOPRESSOR DRUG

In general, a suitable vasopressor is one which restores the circulatory system to its normal pre hypotensive state Some drugs elevate the blood pressure and correct the hypotension, but do not necessarily restore the vascular system to normal For instance, neosynephrine intravenously causes an abrupt rise in both systolic and diastolic pressures, widens the pulse pressure, and slows the pulse (Fig 22) Such a situation in regard to the vascular system did not exist before the hypotension developed The ideal drug is one which restores pulse rate, systolic, and diastolic blood pressures to the pre hypotensive state None accomplish this but some cause less derangement than others In general, ephedrine and desoxyephedrine restore the vascular system to as near a pre hypotensive state as possible as far as blood pressure and pulse are concerned Most vasopressors stimulate the sympathetic division of the autonomic nervous system in such a manner

CLINICAL RECORD — ANESTHESIA

GOOD FAIR POOR

PREMEDICATION

INDUCT

EPHEDRINE 25mg IV

ENDOTRACHEAL

DETAILS OF REGIONAL OR SPINAL

10-2614g 2 ANESTHESIA

FIG 21 The blood pressure after 25 mgm of ephedrine intravenously in a hypotensive state due to spinal anesthesia Note the rather abrupt rise in systolic pressure and the less proportionate rise in diastolic pressure and the increase in pulse rate Note the tachyphylaxis which results from repeated administration of the drug

that side actions such as nausea, vomiting, pallor, dilated pupils, tremors, arrhythmias, and so on occur The drug selected therefore also must be free of side actions

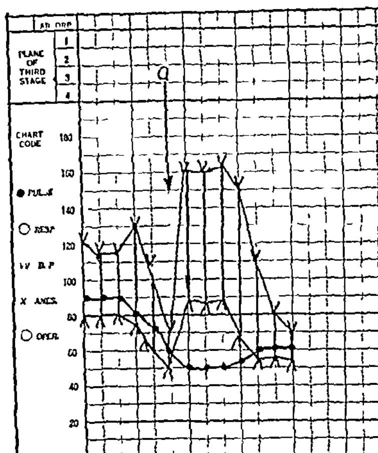



FIG 22 The effect of intravenous neosynephrine upon the blood pressure Note the abrupt rise in systolic and diastolic pressures The diastolic pressure is elevated above the pre-hypotensive level Note the bradycardia which develops This is probably reflex in origin mediated through the carotid sinus *Note the wide pulse pressure and the comparatively brief period of action*

## DETOXIFICATION

The majority of drugs possessing *sustained vasopressor action are slowly* detoxified in the body Epinephrine, and norepinephrine quickly undergo oxidation or deamination *For that reason their action is fleeting* Ephedrine, on the other hand, is slowly destroyed and eliminated which *accounts for the sustained action In a general way* the same is true of other drugs in the group

## REFLEX CIRCULATORY EFFECT

Some vasopressor drugs cause slowing of the pulse, others an increase in rate The bradycardia is most likely due to a reflex stimulation of the carotid sinus as a result of the increased peripheral resistance in the face of an increased cardiac output Neosynephrine behaves in this manner Others cause a bradycardia by vagal stimulation (vasoxyl) Tachycardia is due to stimulation of the cardio accelerator nerves

## USE TO PROLONG LOCAL ANESTHESIA

Although numerous amines have been used for vasoconstriction to pro long local anesthesia, ephineprine is by far the most effective Heretofore, interest in vasoconstrictors was limited to nerve blocking or to local infiltra tion In recent years there has been a growing tendency among anesthesi ologists to combine vasoconstrictors with the spinal anesthetic drug to intensify and prolong anesthesia Controlled studies in man indicate that epinephrine prolongs spinal anesthesia approximately 60 per cent Arte renol acts almost as effectively, being about 10 per cent less effective Pituitrin, which of course is not a sympathomimetic drug, is equally as effective as arterenol In the order of decreasing efficiency are epinephrine arterenol, pituitrin, and neosynephrine Ephedrine, vasoxyl, and oenethyl are of little or no value in prolonging spinal anesthesia Apparently, the pro longation is due to the vasoconstriction which retards absorption of the drug from the subarachnoid space The vasoconstrictor is slowly absorbed from the subarachnoid space The pressor response noted when a drug is in jected intravenously, intramuscularly, or subcutaneously does not occur after intraspinal injection The amount of epinephrine which is effective is 0 25 mgm to 0 5 mgm for every 100 mgm of procaine or an equivalent weight of another drug There is no evidence that the addition of a vasoconstrictor in any way causes neurologic damage or delayed neurologic sequela

## USE AS ANALEPTICS

The stimulating effect on the central nervous system varies with each drug Some, like benzedrine, dexedrine, and metamphetamine have a pronounced effect on the cerebral cortex Others have little or no effect In general it may be said that whatever beneficial responses are obtained in the management of respiratory failure when the sympathomimetic amines are used are due to the peripheral vasoconstriction which improves the cerebral blood flow or to an increase in cardiac output caused by the myocardial stimulation Vasoconstrictors are without effect when the medullary centers are depressed by anoxia, carbon dioxide excess or central nervous system depressants, particularly when cerebral blood flow is adequate

### REFERENCES

ADRIANI J *The Pharmacology of Anesthetic Drugs* 3rd Ed Springfield Thomas 1953 p 105

GOODMAN L and GILMAN A *The Pharmacological Basis of Therapeutics* New York Macmillan 1941 p 396

HENDERSON V E The substances causing vasoconstriction *Anesthesiology 1* 323–340 1940

HOMEYER W MINTZ S ADRIANI J The effects on the duration of spinal anesthesia of combining non anesthetic substances with the agent *Anesthesiology 13* 231–241 1952

# XV

# HYPOTENSIVE ANESTHESIA AND HYPOTHERMIA

A recently popularized innovation of surgery is a technique referred to as "hypotensive anesthesia." Actually the term hypotensive anesthesia is a misnomer. The terms *deliberately induced* or *intentional hypotension* are more accurate descriptions of the technique. As in the case of many supposedly new items in medicine, the technique is a revival of an old established principle. It has been known for some time that sympathectomized animals tolerate blood pressures at shock levels resulting from hemorrhage, without apparent harm for longer periods of time than those whose vasomotor control is intact. The object in intentional hypotension is to interrupt the normal vasomotor control and induce a hypotension to minimize the effects of hemorrhagic shock. This hypotension is induced at a time when massive hemorrhage is anticipated. The technique therefore is one that is adaptable to formidible types of surgery in which uncontrollable hemorrhage occurs or is a possibility. The hypotension supposedly reduces the amount of blood loss due to "oozing."

Inasmuch as the vasomotor control rests with the autonomic nervous system, it is this system which is the site of attack. The autonomic nervous system consists of a plexus of nerves and ganglia, which supply the heart, blood vessels, glands, and viscera. The vascular system is supplied both by vasoconstrictor and vasodilator fibers. A blockade or inhibition of vasoconstrictor impulses or an increase of dilator impulses causes an increase in the cross sectional area of the vascular bed. Presumably the blood volume is not disturbed when this is done. A disparity between the total blood volume and the volume of the vascular space is established. Increasing the total volume of the vascular compartment may be accomplished in a variety of ways. There are a number of sites where one may attack the autonomic nervous system. One may use a drug which acts on the autonomic centers in the midbrain. The sympathetic center located in the hypothalamus transmits impulses which increase vasoconstrictor tone.

A drug which depresses this center reduces the number of impulses and vasodilatation occurs. Apresoline is a drug which acts in such a manner. The use of apresoline for hypotension during surgical anesthesia is not practical however. The sympathetic centers and parasympathetic centers transmit their impulses to the vasomotor center in the medulla. The vasomotor center has vasodilator and vasoconstrictor components. One may cause vasodilatation by using drugs which act upon the vasomotor center. If the vasomotor

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surgery Hexamethonium frequently induces a sustained hypotension which is not easily reversed Ecamon frequently has a fleeting action and hypotension is not easily controlled Two newer preparations which are being studied are Arfonad and Pendiomide Both drugs appear to be controllable and short acting They permit greater control of the blood pressure and prompt reversal of the vasodilatation when it is desired to interrupt it The method of using ganglionic blocking agents is the most popular and the most effective way of inducing controlled hypotension

## SYMPATHOLIC TYPE OF BLOCKADE

If desired the vasodilatation may be obtained by causing a blockade at the nerve endings of the autonomic nervous system A sympatholytic or an adrenolitic drug may be used Dibenamine Priscol, and Benodaine are examples of drugs which cause a blockade at the sympathetic nerve endings Although these drugs are effective, they are used less frequently than the ganglionic blocking agents for inducing hypotension during surgery

## SMOOTH MUSCLE DEPRESSANTS

One may go beyond the nerve endings and administer a drug which depresses the smooth muscle of the vascular bed directly The nitrates and nitrites may be used for this purpose However, they are not controllable or their actions are evanescent, and for this reason hypotensive anesthesia is rarely induced by their use

## ARTERIOTOMY

The blood pressure may also be lowered by reducing the blood volume by employing the procedure known as arteriotomy A canula is placed into the proximal end of the divided radial artery at the wrist The distal end is ligated Blood is withdrawn temporarily into a flask containing an anticoagulant, usually heparin or sodium citrate A monometer is placed in the system so that the blood pressure can be read directly As soon as the need for hypotension is over the blood is re transfused into the artery under pressure Obviously in this method the vascular system retains its vasomotor control and the generalized vasodilatation which is desired in hypotensive anesthesia is not present In due time irreversible shock may occur Frequently when this technique is employed it has been noted that all the blood withdrawn cannot be replaced Presumably this occurs because the generalized vasoconstriction resulting from the hemorrhage has caused the vascular bed to shrink in size Arteriotomy is a tedious, cumbersome procedure and not easily managed Certainly it is not as simple as injecting a drug intravenously as is done when the ganglionic blocking agents are used It must be remembered also that it involves sacrifice of the radial artery

center is depressed, the vasoconstrictor component transmits fewer impulses to the vascular bed, and dilatation occurs Narcotic and hypnotic drugs are used to accomplish this to a certain extent Basal narcotic doses of barbiturates in combination with morphine are used to depress the center This technique has been employed by some otolaryngologists for the fenestration operation The disadvantage of this technique is that the other centers in the medulla, notably the respiratory centers, are depressed along with the vasomotor center

If a drug which stimulates the vasodilator component of the center is used, more impulses are transmitted via the vagus and a dilatation of the vessels occurs The veratrum alkaloids are said to behave in this manner Likewise, they are not of practical use during surgery because of lack of controllability The attack of vasomotor control by influencing the medullary centers, then, is of no practical significance from the standpoint of surgical anesthesia

The pre ganglionic fibers emerge from the spinal cord and pass to the sympathetic ganglia which in turn send post ganglionic fibers to the blood vessels One may attack and cause a blockade of the pre ganglionic fibers as they emerge from the spinal cord No impulses are transmitted and vasodilatation occurs This may be accomplished by inducing spinal anesthesia of the extent referred to as total spinal block In total spinal block the entire cord is bathed by the anesthetic drug Anesthesia extends to the upper cervical segments Respiratory paralysis is managed by using artificial respiration This technique has been used largely by the British Its chief drawback is its lack of controllability The blood pressure often is completely imperceptable and instances of cardiac arrest have not been uncommon Peridural injection of a local anesthetic drug acts in the same manner as subarachnoid injection Larger doses of drugs are required Peridural injections are somewhat more difficult to execute technically The same dangers and lack of controllability exist in this technique as with total spinal block

## GANGLIONIC BLOCKADE

The ganglia themselves may be blocked directly by injecting procaine paravertebrally This is somewhat tedious and is not as effective in securing the generalized vasodilatation which is desired Ganglionic blockade is more effectively obtained by using drugs which act systemically A number of ganglionic blocking agents are available for this purpose It is well known that nicotine, curare, and similar substances cause paralysis of the autonomic ganglia These drugs however are not satisfactory for clinical use More recently hexamethonium or $C_6$ has been introduced to reduce the blood pressure in hypertensive patients Tetra ethyl ammonium chloride (Etamon) has also been used for the purpose Neither hexamethonium nor tetra ethyl ammonium chloride are entirely satisfactory to induce hypotension during

dilator drug is administered intravenously Usually the blood pressure is maintained between 60 to 80 mm Hg If it is maintained above 80 mm Hg the results are not satisfactory Bleeding continues and is not curtailed The technique controls only the ' ooze ' and not the bleeding from major vessels which are severed

## EFFECTS OF POSTURE

The blood in the vascular space is influenced by gravity after the blockade is induced and may be shifted about at will The blood pressure may be reduced further by inclining the patient so that the head is up and the feet are down If the blood pressure falls below the desired depth the head may be tilted downward and the feet raised In this position the effects of gravity cause an increase in the amount of blood returned to the heart and brain and the blood pressure then rises After the denervation is instituted the blood pressure is controlled by varying the position of the patient until the effects of the drug wear off The dose then is repeated It is advisable not to allow the blood pressure to fall below 60 mm Hg Blood must be replaced as lost, otherwise irreversible shock may occur These patients do not tolerate blood loss It is noteworthy that little anesthetic is required during the period of hypotension The depth of anesthesia necessary is nowhere near as great as that which is required without hypotension

## DURATION

The period of hypotension should be as brief as possible, not to exceed one hour as a rule At the conclusion of the portion of the operation requiring the hypotension the blood pressure may be raised by tilting the patient or by injecting a vasoconstrictor drug such as neosynephrin, arterenol, or desoxyephedrine In some cases a combination of tilting and vasopressor drug may be required to restore the blood pressure to normal Fluids are not necessary if blood lost has been replaced Prolonged hypotension increases the incidence of complications The most frequent complication noted in the postoperative period is slow recovery Patients remain in a depressed state for many hours The second most frequent complication is reactionary hemorrhage Bleeding points which have not been detected and ligated before closure may resume bleeding when the blood pressure rises Anuria cerebral thrombosis apoplexy coronary thrombosis and pulmonary embolus have been reported Decerebration and other evidence of damage to the brain due to inadequate blood flow is a possibility and a complication which has been reported

One cannot deny that the technique facilitates the more formidable types of surgery If used with discretion in malignant conditions it is a worthwhile procedure notwithstanding the possible complications It is not an anesthetic procedure by any means The anesthetist merely executes the *technique*

## USES OF HYPOTENSION

As mentioned previously, the chief use of controlled hypotension is for situations in which considerable bleeding is anticipated The hypotension is induced at least 10 minutes prior to the moment the bleeding is anticipated If it is not reduced before this time, it is not always effective A relatively bloodless field results for a brief period so that the surgery may be accom plished with greater ease and with a minimum of blood loss Controlled hypo tension facilitates neurosurgery, particularly when vascular tumors are removed, various forms of plastic surgery, surgery about the head and neck in which bleeding is anticipated, vascular surgery, and radical pelvic surgery In the light of our present knowledge, the technique is best reserved for patients who have malignant disease or benign conditions for which opera tion is a necessity but in which blood loss may cause loss of life

## COMPLICATIONS AND HAZARDS

Obviously there are complications and hazards in using a method of this sort It cannot be employed routinely for every case The relaxation of the vascular bed reduces the blood flow through vital organs If the cardiovascu lar system is diseased, the incidence of complications and untoward reactions and undesirable sequelae mounts Circulation time is prolonged sometimes twice the usual figure If the coronary arteries are diseased, the myocardium does not receive an adequate blood supply and coronary insufficiency follows Some of the fatalities which have occurred during and after the procedure have been due to coronary thrombosis The brain likewise may suffer dam age, due to the lack of nourishment or oxygen deficiency The same patho logic findings found after a period of acute anoxia are noted under these circumstances also The slowing of the circulatory stream in patients who have sclerotic vessels predisposes to thrombosis Emboli may pass to various organs *Emboli are found more frequently in the cerebral vessels* Cerebral thrombosis and coronary thrombosis appear to be the most frequent com plications of the technique

At least 60 mm Hg pressure is necessary to maintain adequate blood flow through the kidney If the blood pressure remains below this level for any length of time filtration ceases and damage to the tubules may result Anuria then follows in the post operative period The picture in these cases is similar to that noted in the lower nephron syndrome Evidence exists that renal dam age appears days after the technique has been used even though function is not disturbed during the operation

## LEVEL AND CHOICE OF ANESTHESIA

In executing the technique the patient is anesthetized in the usual manner preferably with ether or a drug which does not cause vasodilatation Ten to fifteen minutes before the anticipated time of excessive bleeding the vaso

*Local hypothermia (refrigeration anesthesia) is occasionally employed.* Conduction is blocked by cooling a nerve trunk to 4° C. Anesthesia may be obtained by applying a tourniquet to an extremity which is to be ablated and surrounding it with ice for several hours. Anesthesia lasts 20 to 30 minutes after discarding the ice. This is hardly sufficient duration for most operations. The procedure, however, has some merit for poor risk patients in whom delaying an urgent operation would increase the chances of survival. This is so because, in reality, one performs a physiological amputation when using the technique. The absorption of bacterial and other noxious substances from a diseased extremity ceases and one then is free to institute preoperative preparations such as digitalization, administration of blood, restoring fluid balance and so on before proceeding with the operation. The extremity may be kept refrigerated for over 24 hours if necessary without undue harm to the patient.

## REFERENCES

Hampton, J. I., and Little, D. M.: Controlled hypotension in anesthesia. *Lancet 1*: 1299, 1953.

Nicholson, M. J., Sarnoff, S. J., and Crehan, J. I.: The intravenous use of arfonad. *Anesthesiology 14*: 215-225, 1953.

because he ordinarily watches the blood pressure for the surgeon and is in the position to direct its management The procedure is actually one of interrupting the vasomotor fibers to obtain vasodilatation

## HYPOTHERMIA

Central nervous system depressants inactivate the heat regulatory centers The body temperature of an anesthetized patient tends to approach that of the environment In warm surroundings, hyperthermia develops, in a cold environment hypothermia The sweating mechanism ceases to function Cooling no longer occurs by evaporation and body heat is lost only by radiation, conduction or convection Under ordinary circumstances, such as are encountered in hot or cold operating rooms, the body temperature fluctuates 3 or 4°C either way from normal However drastic cooling can be accomplished by the use of ice A recent innovation in surgery is the use of hypothermia as an adjunct to anesthesia Temperatures ranging from 28 to 24°C are attained The metabolism of the tissues is reduced considerably by such cooling This reduction in metabolism is advantageous for surgery in patients who have low arterial oxygen saturation, as for example, that which accompanies certain congenital heart lesions characterized by cyanosis It may make surgery possible in debilitated subjects or in situations requiring temporary occlusion of shunting of blood through a major vessel

The cooling can only be accomplished if anesthesia or basal narcosis is induced with a central nervous system depressant The patient is then cooled by immersion in a tub of ice water or by wrapping in a special blanket composed of coils through which ice water flows or by surrounding the body with ice packs or by placing in a specially constructed refrigerating unit Constant monitoring of cardiac action with an electrocardiograph, continuous recording of body temperature and periodic blood pH determinations are necessary because serious irreversible physiologic disturbances occur as the temperature falls below 30°C Artificial respiration is necessary because spontaneous respiration ceases at 28°C Cardiac irritability increases markedly at 24°C Ventricular fibrillation may occur A respiratory acidosis occurs due to carbon dioxide retention The cardiac irritability and the possibility of ventricular fibrillation are further enhanced by this carbon dioxide retention Forced ventilation is necessary to control the blood carbon dioxide tension The ventricular fibrillation is difficult to reverse once it occurs

Acquired heart disease is considered a contraindication to the use of hypothermia Shivering during the cooling is controlled by administration of additional basal narcotic or anesthetic Shivering predisposes to ventricular fibrillation Frost bite and fat necrosis are possible technical complications from improper cooling Cooling by the use of drugs alone (Thorazine) has been described by certain European workers but appears to be of doubtful practicability

interferes with ventilation and prevents satisfactory lightening and deepening of anesthesia The endotracheal tube obviates these difficulties

## METHODS OF PERFORMING ENDOTRACHEAL ANESTHESIA

The catheter is placed in the trachea by exposing and visualizing the larynx with a laryngoscope The catheter is introduced under direct vision The anesthetist s laryngoscope is similar in principle to that used by laryngologists but is simpler in design The electric current for illumination is derived from standard dry cells used for flashlights These are placed in the handle of the instrument (Fig 23) The blade is flat and broad instead of circular as in the conventional type of laryngoscope used for bronchoscopy This permits visualization of the larynx during introduction of the catheter

The catheter may be introduced through the mouth in which case the procedure is called *oral endotracheal intubation* It may be introduced through the nose in which case it is called *nasal endotracheal intubation* In nasal intubations a catheter is introduced through either nostril into the pharynx Due to the curvature of the catheter and the anatomic position of the larynx the catheter may be passed into the trachea blindly in most circumstances This procedure is called *blind' nasal intubation* Sometimes

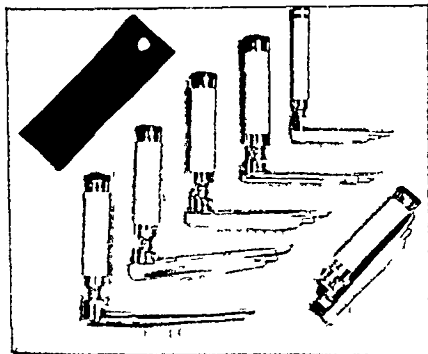


Fig 23 Various types of laryngoscopes used for intratracheal anesthesia. The blades particularly the beak and the curvature have been modified to suit needs in various situations

# XVI

# ENDOTRACHEAL ANESTHESIA

## DESCRIPTION

The term endotracheal anesthesia indicates that a catheter is placed in the trachea during general anesthesia Before the use of non volatile drugs became widespread, the term indicated that inhalation anesthetics were conducted from the inhaler into the trachea through the catheter The primary purpose of the catheter is to provide an airway Actually the catheter extends the trachea to the lips or nares

## USES

During general anesthesia the muscles of the neck, the tongue, the pharynx, and the jaw become relaxed The tongue sags backward As it does the epiglottis swings posteriorly and occludes the pharyngeal passages to the trachea Respiratory obstruction results The catheter provides an unimpeded airway under these circumstances The catheter also permits the anesthetist to exert positive pressure when indicated A smaller inner catheter may be introduced in the tracheal catheter to remove excess secretions This is important during thoracic surgery, particularly in cases of suppurative diseases of the lung One important function of the endotracheal catheter is to prevent laryngeal spasm When the periosteum is incised or traction is made upon the abdominal viscera or upon intrathoracic structures, or when the perineal structures are manipulated or when the rectum is dilated, certain reflexes appear which give rise to respiratory and circulatory disturbances One of the most vexsome features of this reflex activity is laryngeal spasm This spasm interferes with ventilatory functions A catheter placed between the vocal cords obviates this spasm so that anesthesia is conducted uneventfully An endotracheal catheter properly introduced prevents aspiration of vomitus or regurgitated gastric contents This complication is frequently encountered in intestinal obstruction or gastric retention The endotracheal catheter is mandatory for head or neck surgery, because it permits the anesthetist to have control of the airway and still allows him to be out of the operative field For patients undergoing surgery in the prone position, as in the case of operations about the vertebral column back, occipital area and so on the use of an endotracheal tube is mandatory In surgery of the mouth, pharynx larynx and trachea, likewise the use of an endotracheal tube is mandatory Obese individuals and others in whom the airway is maintained with difficulty are best anesthetized with an endotracheal tube in place In upper abdominal surgery, traction reflexes cause laryngeal spasm which

interferes with ventilation and prevents satisfactory lightening and deepening of anesthesia. The endotracheal tube obviates these difficulties.

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The catheter may be introduced through the mouth, in which case the procedure is called *oral endotracheal intubation*. It may be introduced through the nose in which case it is called *nasal endotracheal intubation*. In nasal intubations a catheter is introduced through either nostril into the pharynx. Due to the curvature of the catheter and the anatomic position of the larynx the catheter may be passed into the trachea blindly in most circumstances. This procedure is called "*blind*" *nasal intubation*. Sometimes

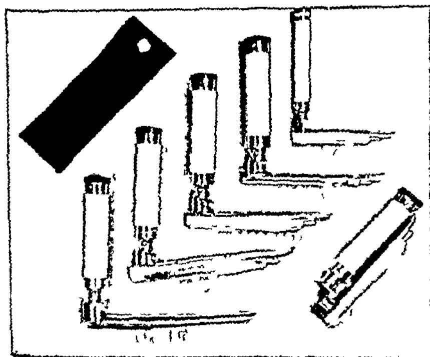


Fig 23 Various types of laryngoscopes used for intratracheal anesthesia. The blades particularly the beak and the curvature have been modified to suit needs in various situations.

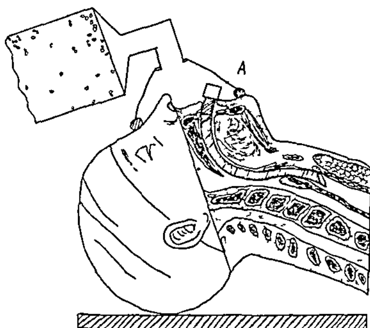



FIG 24 Intratracheal anesthesia by the open oral technique is accomplished by introducing a tracheal catheter by means of direct laryngoscopy replacing the mask and resuming anesthesia in the usual manner No cuff or pack is used. The circle filter the semi-closed inhaler open mask or insufflation technique may likewise be employed instead of the to and fro inhaler shown above

the catheter does not slip in blindly into the larynx, particularly when anatomic deviations exist The larynx is then exposed with a laryngoscope and the catheter is guided into the trachea under direct vision with a forceps After the catheter is introduced into the trachea in the oral technique, an oronasal mask is placed over it and anesthesia is conducted in the usual manner The catheter merely serves as an airway Such a technique is called *open oral endotracheal anesthesia* (Fig 24) When the catheter is placed through the nose and an oronasal mask is applied over the face, it is known as *open nasal endotracheal anesthesia* (Fig 25) The catheter may be connected directly to a closed circle or to and fro inhaler (Fig 26) When this is done the technique is called *closed endotracheal anesthesia*

In order to prevent gases and vapors from escaping through the space between the tracheal wall and the catheter, an inflatable cuff may be used to obtain a tight seal (Fig 27) Some anesthetists prefer to place a gauze pack moistened in normal saline or mineral oil into the pharynx to obtain the seal Cuffs tend to stimulate reflexes, irritate the mucosa of the trachea, denude the epithelium and stretch the trachea In actual practice a perfect seal is not always obtained with a cuff Packs may irritate the pharyngeal mucosa particularly from prolonged contact Like the cuff it also does not always assure a tight seal In the event of regurgitation of vomitus, foreign material passes through the space between the catheter and trachea when the pack is used The possibility of aspiration occurring is less when the cuff is used, although it may happen with either technique Passage of a nasal tube with a cuff

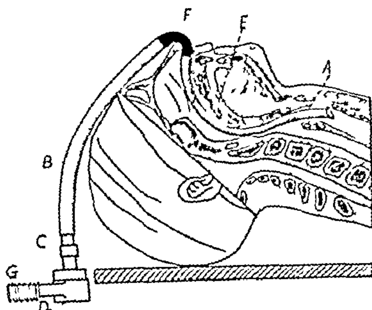



FIG 25 Closed nasal tracheal airway connected to the closed inhaler by means of (F) a metal elbow fitted to (B) a non-collapsible endotracheal tube and (C) a sleeve and (D) a slip joint A gauze pack (E) minimizes leakage of gases and absorbs secretions and blood during the operation

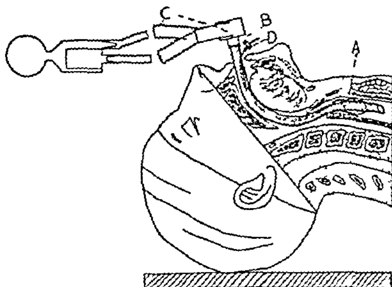



FIG 26 The closed oral endotracheal technique is shown The tracheal airway is connected to a closed inhaler *An inflatable cuff (A) allows a seal to be made between the tracheal wall and* the outside of the catheter so that a completely closed system is secured A slip-joint (B) connects the catheter to the inhaler The diagram depicts a circle filter however a to and fro inhaler may be used equally as well

through the nose is difficult and not practical Packing for nasal endotracheal likewise is not feasible because nasal catheters are soft and are compressed or kinked by the pack as they pass through the oropharynx Packs are used to absorb blood and secretions, however Although the term *closed nasal endotracheal* is used to describe the technique utilizing a nasal catheter and oral pack, it is not strictly correct because the seal is not as complete as it is during oral intubations A large sized catheter which fits snugly into the trachea, may be used to obtain a near leakproof nasal intubation

## TYPES OF CATHETERS

A variety of catheters are used The safest and most practical catheters are known as the *anode* type A thin wire coil is interposed between two layers of thin latex (Fig 27) Such a catheter does not become kinked or compressed on ordinary usage It is atraumatic and easily cleaned and sterilized More rigid catheters are made of woven silk or cotton tubes embedded in plastic substances They are rigid and suitable only for oral use Soft catheters made of ordinary rubber are used more often for nasal intubations rather than oral, though they may be used either way Plastic

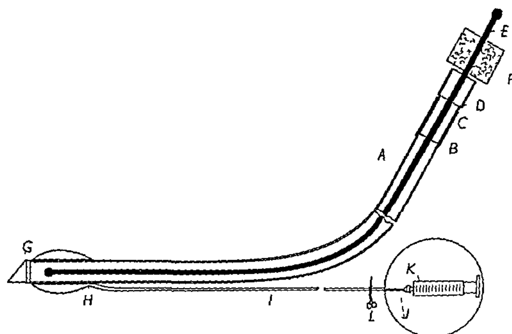



Fig 27 A schematic diagram of a closed oral intratracheal assembly is shown The latex catheter (A) has a wire spiral imbedded in its wall to prevent kinking and collapse The spiral ends at (B) so that section (C) of the catheter may accommodate the metal slip joint (D) Note that the slip joint is introduced as far as the spiral otherwise kinking occurs at this point Internal diameter of the slip joint must be the internal diameter of the catheter Stylet (E) is composed of a stout semi rigid metal rod which is knobbed at either end and fitted with a rubber stopper guard (F) The end of the stylet rests several centimeters from the bevel (G) The inflatable cuff (H) composed of thin latex rubber is provided with a small catheter (I) attached to a 10 cc syringe (K) which is fitted with a short needle (J) A clamp (L) is used to pinch the catheter when the cuff is inflated

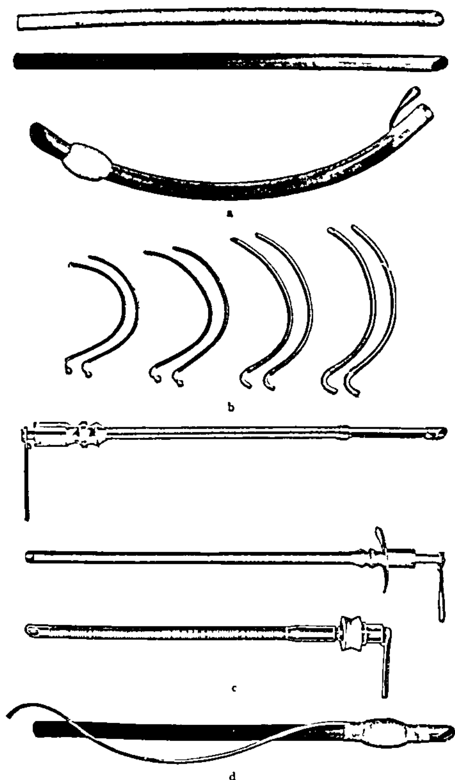



FIG 28 Oro tracheal and nasal tracheal catheters are shown (A) A latex or anode tube with metal spiral imbedded in its wall (B) A plain rubber or Magill nasal tracheal tube (C) A metal Woodbridge tube with a stylet (D) Silk woven catheters

tubes and rubber tubes may become kinked or compressed during use Rigid non collapsible tubes are made of *hard rubber* or *metal* Metal tubes (Fig 28) are of two types, one which consists partly of a solid piece which slips into the trachea and the remainder of a flexible metal coil which passes through the pharynx and is connected to the apparatus (Flagg), and one which is composed entirely of coiled metal (Woodbridge) A thin latex shield is placed over the coiled portion of these tubes to render them airtight

Most catheters vary in size from 3 mm to 1 3 cms in diameter They are numbered according to the French scale (each 3F = 1 mm diameter) The wall of a catheter must be thin to occlude as little of the lumen as possible but it must be sufficiently rigid to prevent collapse and kinking Nasal catheters must be soft to be atraumatic The internal diameter of an intra tracheal catheter must be as wide as possible to avoid any decrease in cross *sectional area of the ventilating passage Catheters average 28 cms in length* for adults If they are too long they may pass into the bronchi, particularly the right one Catheters for infants and children are made of the same materials as those used for adults but must be varied in diameter and length according to age

## ENDOBRONCHIAL ANESTHESIA

For *certain types of surgery, endobronchial catheterization may be re* quired This type of catheterization is used for partial or complete pneu monectomy for suppurative diseases of the lung Secretions and purulent material are thus confined to the diseased portion of the respiratory tract The usual procedure *is to introduce a catheter into the non diseased lung and* completely exclude the diseased lung from the anesthetic system More re cently catheters of the type used for broncho-spirometry (Carlen Tube) have been adapted for anesthesia. Catheterization of both lungs simultaneously is thus possible This is really two endobronchial catheters fused together in the tracheal portion The division into a right and left branch is at the carina Each division passes into the right and left bronchus, respectively

## TYPE OF ANESTHESIA NECESSARY FOR INTUBATION

The secret of successful endotracheal or endobronchial intubation is to have the patient completely relaxed so that the larynx may be readily ex posed and visualized In order to accomplish this, a major anesthetic must be used The cough reflex in the trachea and bronchi must be abolished The pharyngeal reflex disappears in the first plane of third stage anesthesia, the laryngeal and tracheal in second plane, and the reflexes in main stem bronchi in third plane. Consequently nitrous oxide, ethylene, and vinyl ether are not satisfactory for endotracheal intubation Ether, cyclopropane, or other anes thetics which abolish these reflexes must be used Non volatile drugs such as avertin and thiopental are not satisfactory because they do not abolish the

tracheobronchial reflexes As a matter of fact, thiobarbiturates increase the activity of these reflexes Laryngeal spasm results and the catheter cannot be introduced without undue trauma In the event the catheter is successfully passed, intense bronchial spasm may be initiated

In cases where obstruction of the air passages exists or the development of obstruction is anticipated during induction, the catheter is placed in the trachea using topical anesthesia before general anesthesia is induced while the patient is conscious Then anesthesia is induced in the usual manner Edema of the larynx or pharynx, a deviated trachea or tumor masses of the neck cause such a difficulty and require preanesthetic intubation In cases in which a *tracheotomy* is present, the apparatus may be connected directly to the cannula by means of an adapter and anesthesia is conducted in the usual manner Such a technique is actually endotracheal anesthesia

The use of the muscle relaxing agents for intubation has had a two-fold effect (1) It has simplified intubation, and (2) it has led to the abuse of endotracheal intubation In localities where anesthesia is technically poor it is common practice to combine a muscle relaxant with a thiobarbiturate or other basal narcotic No volatile drug is used Obviously the patient cannot protest or resist because the muscles are flaccid and he is narcotized from the barbiturate However, the tracheal and the bronchial reflexes are not abolished Circulatory changes or broncho pasm may occur from intubating in this manner In addition excessive amounts of both drugs are necessary to accomplish the intubation Prolonged depression may follow in the postoperative period One of the most satisfactory techniques for intubation is to use a basal narcotic and then anesthetize the patient with cyclopropane or ether At the time of attempted intubation a muscle relaxant is administered Succinyl choline is ideal for this purpose Anesthesia is then maintained as usual Intubations, of course, may be performed using chloroform also, but this agent is no longer used in the United States

## ADVANTAGES AND DANGERS OF INTUBATION

Perhaps no refinement in modern medicine has added so much to the safety of anesthesia as endotracheal intubation However, complications may arise as a result of faulty technique The harmful effects of reflex activity have been mentioned If the intubation is performed using light anesthesia "bucking" elevates the venous pressure and induces "circulatory strain" Intubation sometimes causes an apnea which is reflex in nature This probably is due to vagal stimulation and inhibition of the inspiratory centers Trauma perhaps accounts for the greatest number of complications Trauma results from using force in passing catheters or exposing the larynx with the laryngoscope Gentleness is absolutely essential Most trauma is inflicted when the anesthetist attempts to rush the intubation or if the patient is not sufficiently anesthetized and relaxed Trauma to the mucosa and to the

pharynx is common Rupture of the pharynx or trachea and tearing of the vocal cords are complications of endotracheal anesthesia seen from time to time The mere fact that an endotracheal tube has been inserted does not necessarily insure against respiratory obstruction The tubes may become kinked, filled with secretions, blood, or purulent material They may become compressed, particularly if they are of the soft rubber type

In infants, particularly if sterile technique is not used, even slight trauma may cause edema of the larynx in the postoperative period Most anesthetists prefer not to intubate children unless absolutely necessary When properly done with the proper equipment, there should be no objection to the use of endotracheal anesthesia in children

Fibroma of the vocal cords has been blamed upon endotracheal anesthesia, but whether or not this is the causative factor has never been established The complication is rare Teeth may be broken and the tongue may be cut or bruised by technical incompetence or difficulty Occasionally one hears a physician state that he does not "believe" in endotracheal anesthesia These doctors know little or nothing concerning anesthesia Endotracheal anesthesia is not a doctrine but a "must" If asphyxia is to be prevented, there are certain cases in which it is mandatory Certainly, there are disadvantages but the advantage of increased safety far outweighs any disadvantages

## CONTROLLED RESPIRATION

It is common practice to deliberately induce apnea during general anesthesia This is often necessary during thoracic and abdominal surgery to facilitate the procedure by providing a "quiet" abdomen or mediastinum when movements of the viscera interfere with surgical manipulations The anesthetist then breathes artificially for the patient by compressing the breathing bag of the apparatus rhythmically and intermittently to inflate the lungs Expiration is passive The procedure is called *controlled respiration* Endotracheal intubation is necessary to safely and adequately execute controlled respiration The inhaler is connected directly to the catheter

The apnea is induced in a number of ways The most common way involves a combination of several drugs Usually drugs which depress respiration, such as the narcotics or the barbiturates, are used with cyclopropane Resipration is depressed by the combination The manipulations of the breathing bag are carried out forcibly, at first, so that the Herring Bruer reflex inhibits respiration by distending the alveoli This inhibitory reflex is easily activated in the face of the existing depression In addition, the forced ventilation reduces the alveolar and blood carbon dioxide tension below the critical level necessary to stimulate the respiratory center These three factors, central depression, inhibition of the inspiratory reflexes and removal of the normal stimulus to respiration, cause the apnea Drugs which stimulate the pulmonary vagal receptors, such as ether or chloroform, are not suitable for inducing

apnea in this manner When ether is used the apnea is short lived unless the blood level is raised to the point which paralyzes the central receptors—a dangerous practice When depressant drugs are not desired a muscle relaxant is used to completely paralyze the intercostal muscles and the diaphragm Although not a practical method of inducing apnea, respiratory movements cease during hypothermia if the critcial level of 28°C is exceeded

The effect of prolonged positive pressure on the airway may be detrimental because the venous return to the heart is impaired A reduction in cardiac output may induce serious peripheral vascular stasis A number of mechanical ventilators have been devised to automatically ventilate the lungs during operation These devices are still in the experimental stage, and, for the moment, are tools for the clinical investigator

## REFERENCES


ADRIANI J *The Techniques and Procedures of Anesthesia* Springfield, Thomas 1946, pp 111–137

BRACE D E. REID L. C Reflexes from the mouth and esophagus and trachea which stimulate respiration. *Anesthesiology 4* 345–355 1943

BURSTEIN C L *Fundamental Considerations in Anesthesia* New York Macmillan 1950

COLLINS V J *Principles and Practice of Anesthesiology* Philadelphia Lea & Febiger, 1952

CULLEN S *Anesthesia in General Practice* Chicago Yr Bk. Pub, 1946

GILLESPIE, N A. and CONROY W A. *Endotracheal anesthesia the relation of nasal* tracheal and oral tracheal intubation to respiratory morbidity *Anesthesiology 2* 28 1941

GILLESPIE N A. *Endotracheal Anesthesia.* Madison Univ Wisconsin Press 1948

GUEDEL A. E *Inhalation Anesthesia* New York Macmillan 1950

GUEDEL A. E. and WATERS R. M A new intratracheal catheter *Anesth & Analg 7* 238 1938

KING B D HARRIS L C GREIFENSTEIN F E EIDER J D JR. DRIPPS R. D Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. *Anesthesiology 12* 556 566 1951

LUNDY J S *Clinical Anesthesia* Philadelphia Saunders 1942

XVII

# CAUSES OF OPERATING ROOM DEATHS

Most fatalities which occur during or immediately after general anesthesia which can be ascribed solely to anesthesia are due to *asphyxia* Next in order of importance are fatalities due to *overdosage* The combination of overdos age and respiratory obstruction also accounts for a large share of the deaths Fatalities due to *untoward reactions* of drugs or misuse of drugs occur less frequently, but also account for some mishaps

Many fatalities ascribed to anesthesia are shown by careful postmortem examination to be due to *causes not related* to anesthesia Pulmonary emboli due to clots, air, or fat head the list of causes of sudden death not due to anesthesia Cardiac arrest from coronary artery disease is next in order of importance Other forms of cardiac disease are less common causes of sudden death Severe untreated shock or irreversible shock occurs often during surgery but rarely causes sudden death Death is usually delayed in such instances The surgeon and the anesthetist are forewarned of the impending catastrophe and it comes as no surprise Cerebral accidents are uncommon, during operation They may be precipitated by some factor concerned with anesthesia or some technical mismanagement of anesthesia However they do not usually cause death on the operating table Sudden massive hemor rhage particularly if unrecognized, may account for some fatalities As a rule, though, death is delayed, as in the case of shock Adrenal insufficiency, although uncommon, has been known to cause sudden death during opera tion

In the absence of postmortem examinations many fatalities occurring on the operating table are ascribed to obscure highly speculative causes The mythical status lymphaticus has in the past provided an excuse and a simple explanation for many deaths due to technical anesthetic errors This syn drome is no longer accepted as a clinical entity by most clinicians If it does exist it is doubtful that it is the causative factor in anesthesia deaths Another over emphasized and convenient alibi for technical errors during anesthesia is the vago-vagal reflex Controversy exists concerning the relationship between this reflex and sudden death during surgery The occurrence of this reflex cannot be denied However, how frequently it causes death is another matter One school of thought feels that vago vagal reflexes do occur but do not cause death except in the face of acute anoxia In well ventilated subjects, when oxygenation is adequate and no disturbance of acid base balance exists, sudden death seldom occurs irrespective of the intensity of the offending vagal stimulus The writer subscribes to this view

Most fatalities resulting from anesthesia are unexpected and usually occur suddenly, almost without warning Some are delayed however and occur during the recovery period Some postoperative deaths result from insidious processes which are not related to anesthesia but which are initiated during the operation Others result from some catastrophe which occurs during anesthesia and carries over to the postoperative period

## FATALITIES DUE TO ANOXIA

Fatalities due to asphyxia result from (1) *a reduction of the oxygen tension* of the inhaled mixture below the amount necessary to maintain life, (2) *obstruction* to respiration, and (3) Decreased tidal exchange or *hypoventilation* from respiratory depression or respiratory paralysis When the inhaled oxygen tension is reduced to dangerous levels death apparently is due to anoxic anoxia Carbon dioxide excess and anoxia both play a role in deaths from obstruction and hypoventilation In cases when death results from hypoventilation the respiratory acidosis may be the causative factor and not the suboxygenation Experimentally, ventricular fibrillation has been precipitated by stimulation of the heart, vagi and other structures during respiratory acidosis even though no anoxia was present

Inasmuch as overdosage of a central nervous system depressant causes paralysis of the respiratory centers, most deaths due to that cause are asphyxial deaths It is possible with most anesthetic drugs to induce respiratory failure and still sustain life by artificial respiration The lethal dose is greater than the dose which causes respiratory failure Accidents due to administering inadequate concentrations of oxygen are due to many causes Defective apparatus may fail to deliver the necessary gas flow even though the instruments indicate an adequate flow Inadvertently placing the wrong gas cylinder on the yoke of the oxygen cylinder has caused accidents Helium, nitrous oxide and ethylene cylinders have been mistaken for oxygen and the error has resulted in fatalities Gases of low potency which necessitate high partial pressures in the alveoli to obtain surgical anesthesia may be administered in concentrations above their safe limit, particularly when used for resistant individuals Death then occurs from anoxic anoxia This type accident has been emphasized in the discussions under nitrous oxide and ethylene It may also occur when vapors of volatile liquid anesthetics are mixed with air in the open and insufflation techniques The oxygen is diluted below the safe level and anoxia results

In anemic individuals a partial pressure of oxygen in the inhaled mixtures, which ordinarily would be tolerated without harm by the average person, may be fatal Inexperienced anesthetists who rely upon cyanosis as a guide to the degree of oxygenation may be deluded into a false sense of security when anesthetizing anemic patients because cyanosis does not appear in these subjects until near fatal anoxia is present Deaths due to "demand

hypoxia" are infrequent In these cases the anesthetist fails to administer sufficient oxygen to compensate for any increase in metabolic oxygen requirement during maintenance of anesthesia

## FATALITIES DUE TO OBSTRUCTION

Obstruction accounts for many asphyxial deaths The majority of these are due to aspiration Vomiting, whether it occurs during the induction period, the maintenance phase, or at the conclusion of anesthesia accounts for most aspiration The patient with a full stomach is one of the poorest surgical risks from the standpoint of anesthesia Irrespective of the type of anesthetic desired, whether it be local, intravenous, inhalation or spinal, a patient who has a "full stomach" invariably vomits during or after surgery, and aspirates If the gastric contents are fluid, drowning occurs, if solid, they are drawn into the trachea and bronchi, and obstruction results Any patient in the supine position who vomits invariably aspirates the vomitus Many clinicians have the erroneous impression that a patient being operated upon under spinal, local or nerve block anesthesia cannot aspirate because the cough reflex is not abolished Irrespective of the activity of the cough reflex the supine position favors aspiration As a matter of fact the patient undergoing surgery is not in a position to sit upright if he vomits during the procedure He aspirates irrespective of the activity of the cough reflex

Whenever possible the operation should be postponed if the patient has recently partaken of food Gastric lavage is of questionable value Often the situation is made worse by lavage because more of the lavage fluid is retained than is returned Emetics, likewise, are of questionable value The only recourse the anesthetist has to prevent aspiration when vomiting occurs is to tilt the patient in a steep head down position and rely upon a well functioning suction apparatus to remove the vomitus Normally the stomach empties in approximately four hours This is not so in surgical patients however Apprehension, medication and other factors may delay the emptying time of the stomach for as long as a dozen hours Regurgitation of gastric contents is not an uncommon occurrence when intestinal or pyloric obstruction are present Regurgitation and aspiration are more frequent when a gastric tube is in place during operation because the patient regurgitates around the tube and aspirates The skill of the anesthetist is of importance in these situations Often vomiting and retching is initiated by prematurely introduced airways or by allowing the patient to become light

Purulent material suddenly released from a lung abscess as a bronchiectatic cavity may occlude the large bronchi or pass into the healthy portions of the lung, thereby causing asphyxia Hemoptysis, occurring in patients who have tuberculosis or bronchiectasis, may likewise cause fatalities by drowning Excess secretion of mucus from inadequate pre medication or the omission of the belladonna alkaloids also contributes to fatalities due to obstruction

The most frequent cause of asphyxia is obstruction of the airway Although this occurs in a number of ways it most frequently results from the relaxation or "swallowing" of the tongue and structures in the anterior portion of the pharynx "Swallowing the tongue" is actually a falling backward *of this muscular organ as it becomes relaxed and loses its tone The epiglottis* then falls backward and causes obstruction by partly occluding the glottis A pharyngeal airway or "throat tube" is introduced to support these structures (Figs 29 and 30) In obese individuals it is difficult to maintain a com

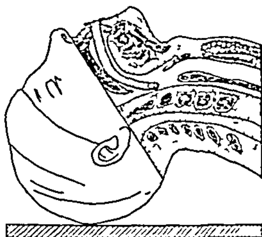


Fig 9 Oropharyngeal airway in position Note that the airway does not extend beyond the hypopharynx

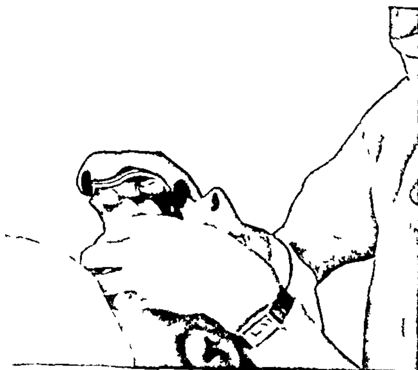


Fig 30 Insertion of the oropharyngeal airway The airway is held in the horizontal position and swept into the pharynx with a rotary motion

pletely patent airway because the epiglottis is short and the tissues in the neck are abundant and flabby Distortions or encroachments upon the airway from edema (Ludwig's angina), excess lymphoid tissue, tumor masses, an enlarged thyroid gland, and laryngeal polyps are common causes of obstruction Foreign bodies in the airway such as sections of bridgework, chewing gum, pieces of tonsil tissue, blood clots, solid food particles and the like may cause obstruction and fatal asphyxia

Vocal cord paralysis, particularly when bilateral, causes obstruction Laryngeal and bronchial spasm are often blamed for causing death by asphyxia The possibility of death from this cause cannot be denied How ever when such fatalities are studied closely, evidence of obstruction, besides the spasm, is uncovered As the spasm is released the patient makes a sudden pronounced *inspiratory effort If obstruction is present from a relaxed* tongue, secretions or a foreign body and ventilation is inadequate at this moment death swiftly follows from asphyxia

Certain fatalities from obstruction result from the inability of the anesthe tist to maintain a patent airway because the patient is placed in an awkward position When the lateral or prone positions are necessary an adequate air way is assured only by a properly placed endotracheal catheter It is almost impossible for the anesthetist to safely maintain an adequate airway for operations performed in the head and neck areas without an endotracheal catheter

## FATALITIES DUE TO DEFECTS IN APPARATUS

Mechanical factors due to defects in apparatus may be responsible for asphyxial deaths Kinking, compressing, plugging or improper placement of endotracheal tubes cause obstruction Defects in the valves and tubing of the inhaler, or improper use of shut off valves may interfere with ventilation and cause asphyxia

## FATALITIES DUE TO HYPOVENTILATION AND OVERDOSAGE

Hypoventilation causes both anoxia and a retention of carbon dioxide De pression of the respiratory center by the drug may initiate a vicious circle which is augmented by the concomitant anoxia and carbon dioxide excess Fatalities may occur when hypoventilation develops in the prone, lateral or other awkward position and the feeble expiratory excursions are impeded by the posture Overdosage must be promptly recognized and corrected by artificial respiration If not recognized, death results from asphyxia The simpler it is to administer an anesthetic, or the more potent and rapid acting a drug is, the easier it is to attain a lethal concentration One of the safe features of ether is that it can only be administered at a given rate and in a concentration which can only be increased gradually to the patient's toler

ance Cyclopropane and thiopental are more dangerous than ether in this regard Overdosage from rapid administration may occur easily when the latter are used

Fatalities due to overdosage often result from nonchalance on the part of the administrator In these days of techniques embodying the use of deliberately induced apnea, respiratory arrest due to overdosage is often mistaken for one due to a reflex or acapnia, and the patient dies

## FATALITIES DUE TO UNTOWARD REACTIONS OF DRUGS

Surprisingly, untoward reactions to drugs account for comparatively few anesthetic deaths Anesthetic drugs which increase cardiac irritability may cause death particularly when administered simultaneously with non anesthetic drugs such as epinephrine *Halogenated hydrocarbons may cause cardiac depression and asystole before medullary depression* The blood concentration necessary to depress the heart is equal to that or even less than that which is necessary to depress the medulla Intolerance to non volatile drugs such as barbiturates has been responsible for some fatalities *In all* instances in which the drug is incriminated, more often than not, it is the abuse, rather than the use, which causes fatalities The widespread use of combinations of non volatile drugs, relaxing agents and inhalation anesthetics multiplies the hazards of each drug

## RELATIONSHIP OF FATALITIES TO CONDUCT OF ANESTHESIA

Most fatalities occur either during the induction period or at the conclusion of anesthesia They are less frequent during the maintenance phase There are a number of reasons for this frequency at these times Vomiting is more apt to occur during the induction period Asphyxial concentrations of induction agents such as nitrous oxide or ethylene are given at this time Patients who become easily obstructed or whose airway is difficult to establish do so early and are asphyxiated at this time Once anesthesia has been established and the difficulties of induction overcome matters than continue smoothly in most cases If complications develop during the maintenance phase nonchalance, carelessness or thoughtlessness are often the underlying factors responsible

It must not be assumed however that the maintenance phase of anesthesia is completely without danger Failure to continue to maintain an adequate airway and overdosage are the two most frequent technical difficulties encountered during maintenance Overdosage *alone is not* a frequent cause of death unless the anesthetist is thoughtless, inattentive, and does not institute artificial respiration immediately when it occurs The chances of resuscitation when overdosage occurs *in* combination with anoxia, hypercapnia or shock are decreased The medullary paralysis may be difficult or impossible

to reverse Death may occur promptly if any one of these factors complicates overdosage

As in the case of induction of anesthesia, the period immediately following the conclusion of anesthesia and the immediate post anesthetic period are fraught with danger The majority of anesthetic deaths appear to occur at this time Again asphyxia from one cause or another appears to be responsible Aspiration, obstruction, premature removal of the pharyngeal or intratracheal airways, swallowing of the tongue and laryngeal spasm are the usual causes There is a tendency for members of the operating team to relax their vigilance at this time and for senior members of the surgical staff to relegate the patient to the care of less experienced individuals The thoughtless anesthetist neglects the patient to complete the chart, to arrange for details for the next anesthetic or to attend to other comparatively trivial chores The careful anesthetist observes his patient closely until all reflexes have returned and the possibility of respiratory obstruction has passed During the immediate post anesthetic period the anesthetist must be prepared to deal with respiratory obstruction, emesis and other possible complications

## FATALITIES DUE TO INTRAVENOUS USE OF DRUGS

Irrespective of the method of induction of anesthesia or narcosis, whether it be by inhalation, intravenously or rectally, as long as it is attended, a loss of consciousness the danger from asphyxia exists The intravenous administration of central nervous system depressants, combined with muscle relaxants and inhalation anesthetics, is popular practice "Intravenous anesthesia" has gained popularity since the introduction and development of the ultra short acting barbiturates "Intravenous anesthesia" has considerable appeal because it may be simply induced and maintained even by the unskilled and uninitiated Unfortunately this simplicity of induction and maintenance appeals most to those who know least about the hazards of anesthesia and to those who tend to regard anesthesia lightly

The practice of maintaining anesthesia with ultra short acting barbiturates alone has long been abandoned in up to date medical centers Today the barbiturates, when correctly employed, are used solely for basal narcosis They are neither analgesic nor do they provide the muscle relaxation necessary for surgery Used without an analgesic, a cumulative action characterized by distressing circulatory and respiratory depression and prolonged somnolence follows Individuals who are not versed in the fundamentals of anesthesiology and who are not aware of the hazards of anesthesia invariably concentrate their attention on the intravenous injection The airway is the least of their concern and obstruction results Asphyxia from obstruction is as great a hazard during intravenous anesthesia as inhalation anesthesia

Many fatalities occur when the ultra short acting barbiturates are used

for head and neck surgery Intravenous anesthesia is selected for operations about the head and neck by those unfamiliar with the hazards of anesthesia because the anesthetist may be removed from the operative site The fact that *the patient must breathe is given no thought* The anesthetist cannot possibly have control of the airway under these circumstances A few surgeons, for reasons known only to themselves, are reluctant to use endotracheal anesthesia In these situations in which the airway cannot be controlled an endotracheal catheter is mandatory Unless these patients are intubated in these situations one is inviting disaster

## FATALITIES DUE TO MUSCLE RELAXANTS

The muscle relaxants are widely used today It has been assumed that fatalities following the use of muscle relaxants are due to asphyxia resulting from respiratory paralysis However, a toxic dose exists for each of these drugs which is, in most instances, greater than the curarizing dose In dogs, even if adequate artificial respiration is maintained, a dose five times the curarizing dose causes death from circulatory failure In a study of anesthetic deaths over a five year period Beecher has noted a mortality of 1 to 370 when a muscle relaxant was used as an adjunct to anesthesia in contradistinction to 1 in 1500 when a muscle relaxant was not used This data is of a preliminary nature but merits some study It is Beecher's impression that some inherent toxicity of the drug exists which is as yet unrecognized in the laboratory or clinically

## FATALITIES DUE TO SPINAL ANESTHESIA

Regional anesthesia also has its set of hazards Spinal anesthesia is ideal for many types of surgery but when misused is hazardous The mortality from spinal anesthesia is shamefully high in the light of our present knowledge It cannot be denied that spinal anesthesia provides relaxation which cannot be duplicated by any other method The desire for this extreme degree of relaxation clouds the judgment of many an operator and leads to the selection of spinal anesthesia in subjects who are unable to withstand the physiologic disturbances following its induction Death from spinal anesthesia has been described under that heading (Page 121) It is usually caused (1) by respiratory paralysis or (2) circulatory failure Both of these complications appear early in the course of anesthesia

The respiratory paralysis results from ascent of the drug into the upper thoracic and cervical portion of the spinal canal Paralysis of the intercostal muscles and the diaphragm follows If immediately recognized this complication need not be serious However, if not recognized or if it is over looked and not treated until the circulation fails, death results from asphyxia The attentive anesthetist closely observes both the respiratory exchange and the status of the circulatory system after inducing spinal anesthesia Respira

tory paralysis is easily overcome by artificial respiration by an instantly available method Much nonsense has been written about paralysis of the vital centers which follows the ascent of the drug into the medullary area Long before this occurs respiratory paralysis ensues because the drug affects the intercostal and phrenic nerves first Death from this complication usually occurs in the hands of the occasional spinal anesthetist who neither recognizes the complication nor knows how to manage it when it occurs

The majority of deaths from spinal anesthesia are from circulatory col lapse It is a matter of common knowledge that a hypotension accompanies spinal anesthesia The mechanisms causing it are described in the discussion on spinal anesthesia (Page 116) The severity of the circulatory disturbances increases as the number of dermatomes anesthetized increases Fortunately this complication is readily overcome with vasopressor drugs Some oper ators disregard the hypotension when it appears In robust subjects mild disturbances right themselves without ill effects Severe disturbances if un treated progress to the point of complete respiratory paralysis and circula tory failure and death In certain instances patients have been revived by cardiac massage However severe damage to the cerebral cortex and other parts of the brain has resulted from the anoxia caused by the temporary arrest of the circulation Pre existing disease of the circulatory system in creases the hazard of spinal anesthesia Patients with myocardial disease, anemia, or hypotension are, as a rule, poor candidates for spinal anesthesia

## FATALITIES DUE TO LOCAL ANESTHETIC DRUGS

The question of the toxicity of the drug invariably arises when an accident occurs in attempting spinal anesthesia Although it is possible for a reaction to occur from the accidental intravascular injection of the local anesthetic drug used to induce spinal anesthesia, such mishaps are rare The dose employed for spinal anesthesia is minute compared to the amounts used for *nerve blocking and infiltration The amount of a local anesthetic drug* neces sary for a spinal block even if given intravascularly would be insufficient to cause a reaction, let alone to cause a fatality

Accidents, of course, occasionally may follow infiltration anesthesia and nerve block These reactions have been described under the section on local anesthesia There is a deep rooted impression in the minds of most physi cians that local anesthesia is the safest and best for poor risk patients Although generally true, shock and other complications of surgery may occur as readily during surgery performed with local anesthesia as with general anesthesia Then, patients whose circulatory system is deranged, do not withstand the depressant effect of even less than the average amounts of local anesthetic drugs as do normal individuals The safety of local anes thesia is more apparent than real Only simple palliative procedures may be performed using local anesthesia by the average surgeon As a result as little

as possible is done to poor risk patients General anesthesia permits surgery of a greater magnitude Often surgeons do more than the patient is able to withstand when general anesthesia is used

## RESPONSIBILITY OF THE ANESTHETIST IN PREVENTING DEATHS

The anesthetist who does not attend to the patient constantly while administering an anesthetic is a dangerous individual An anesthetist who walks about in the operating room, gazes out of the window or leaves the room to smoke or for a telephone call is a thoughtless one A capable surgeon, aware of the fundamentals and hazards of anesthesia, expects nothing more of an anesthetist than the administration of the anesthetic He appreciates the constant vigil of a conscientious anesthetist Too often the anesthetist is asked to perform tasks incidental to but not related to anesthesia which takes him from his patient Such distractions have been responsible for fatalities or near fatalities Constant attendance of the patient under anesthesia, regardless of the type, must be practiced by responsible individuals Such tasks as starting infusions and transfusions, shifting of lights, cranking the table, are none of the anesthetist's concern and should be relegated to other members of the operating team, unsterile nurses or orderlies

It is not the scope of this section to include other than the most obvious hazards of anesthesia In studying anesthetic deaths it is remarkable how frequently an anesthetist in stating the sequence of events leading to the accident relates "the patient was doing well but all of a sudden he stopped breathing and we could not feel the pulse" However, it is also interesting to note upon further questioning that the significant prodromal signs were not recognized Changes in the character of respiration and the quality of the pulse, in the activity of the reflexes or in the status of the neuromuscular system, any of which are significant warnings of impending disaster to an experienced observer, were overlooked Failure to observe and heed these warning signs is not necessarily due to thoughtlessness or neglect, but rather to a lack of experience or knowledge of the science of anesthesiology Unless one who administers anesthetics has knowledge of human physiology and of the pharmacology of anesthetic drugs, and is familiar with the patient's disease and how it is affected by the drugs, surgery and other factors, he is merely a technician and not an anesthesiologist

## CARDIAC ARREST

It has been said that the incidence of cardiac arrest on the operating table is increasing The writer feels this increase is more apparent than real Five or six years ago physicians hesitated in opening the chest and massaging the heart when cardiac arrest was suspected This situation no longer holds

Today if there is any indication whatever that cardiac arrest has occurred, surgeons immediately open the chest and attempt to resuscitate the heart The procedure itself adds drama to the episode

Situations which may lead to cardiac arrest are increasing in number however Some of the factors concerned with this increase are (1) More intrathoracic surgery is being performed, not only on the lung but on the heart and the great vessels Factors precipitating cardiac arrest are greater in this type of surgery (2) Refinements in anesthesia and control of blood volume have placed surgeons at ease during operation Operators in training no longer are learning to operate rapidly Consequently four, five and six hour procedures are not uncommon Irrespective of their apparent good condition patients are on the table too long (3) The widespread use of combinations of drugs, particularly the non volatile drugs, may have a bearing on the increased incidence of anesthetic deaths (4) An increase in the life expectancy of the population as a whole has resulted in increase in the number of surgical patients in the upper decades Many of these have well advanced degenerative diseases and cannot withstand the surgery under taken

The results of cardiac massage and defibrillation are disappointing as a rule Unless performed immediately cerebral damage invariably results if the patient survives Prevention should be the goal rather than cure

## REFERENCES


Adriani J Deaths from anesthesia *M Times New York 80* 329 1952

Carron H Prevention and treatment of anesthetic accidents *J Florida M A 40* 93, 1953

Green Barnett A. The hazard of fire and explosion in anesthesia *Anesthesiology 4* 144 1941

Guedel A. E *Inhalation Anesthesia* New York Macmillan 1950

Pender, J W and Essex H. E. A study of traumatic shock under certain anesthetics *Anesthesiology 4* 247 252, 1943

Slocum H. C Hoeflich E. A. and Allen C R. Circulatory and re piratory distress from extreme position on the operating table *Surg Gynec & Obst, 84* 1051 1947

Symmers D Status lymphaticus *Am J Surg 26* 7 1934

# PART II

# RELATIONSHIP OF ANESTHESIA TO NON-SURGICAL DISEASES COMPLICATING SURGERY

XVIII

# CARDIOVASCULAR DISEASE

## HEART

Cardiovascular diseases comprise the largest group of medical complications encountered in surgical patients Each year due to the lengthening of the life span a greater number of patients in the older age group come to surgery It is in this group that the so called degenerative diseases are most prevalent Among these degenerative diseases cardiovascular disturbances pose the greatest problem for the anesthetist

Anesthesia may affect the cardiovascular system in a number of ways (1) By depressing the myocardium and thereby decreasing the cardiac output (2) By increasing cardiac irritablity and thereby causing disturbances in rhythm (3) By increasing or altering the vagal or sympathetic activity, thereby changing the rate and rhythm (4) By increasing epinephrine output thereby increasing the irritability (5) By altering the peripheral resistance by central or peripheral effects thereby changing the blood pressure and blood flow (6) By prolonging circulation time thereby affecting nutrition of cells (7) By reducing venous return to the heart thereby affecting cardiac output (8) By altering capillary permeability thereby causing changes in blood volume

Then, also, the secondary effects upon the circulatory system caused by depression or stimulation of respiration must be considered Some anesthetics, though they themselves have little direct effect on the cardiovascular system, indirectly exert an influence by affecting other physiologic systems Changes in the respiratory system are reflected secondarily, often with serious consequences, in the circulatory system

In general, nitrous oxide or ethylene without anoxia, ethyl ether, vinyl ether and basal narcosis with barbiturates used judiciously are the more desirable choices when cardiovascular diseases coexist with a surgical disease Regional anesthesia may be satisfactory in properly sedated non apprehensive patients It is less desirable than general anesthesia or is to be avoided in excitable non cooperative subjects It is frequently used in moribund or comatose or extremely ill patients in whom surgery cannot be deferred Less desirable and to be avoided are chloroform, ethyl chloride, trichlorethylene and other halogenated hydrocarbons Cyclopropane and spinal anesthesia are used by some Whether or not it should be used depends upon the type of cardiovascular disease In general they are also best avoided, the former because of its effect on rhythm, the latter because it

causes hypotension Drugs or techniques which cause respiratory depression leading to anoxia or carbon dioxide retention are to be scrupulously avoided Excitement and struggling are determinental to any patient let alone the one who has heart disease Stormy prolonged induction of anesthesia therefore is to be avoided

The supposed effects of anesthesia on the cardiac patient are frequently emphasized with the inference that the anesthetic is the injurious agent and the surgery is not Often the question posed is how well will a patient with cardiovascular disease withstand anesthesia when actually it should be how well will he withstand the operation together with the anesthetic Obviously the nature of the cardiac disease has considerable bearing on the entire problem of operation and anesthesia The practice of labeling a patient a "cardiac" and managing each case in a routine fashion is a common one and one which should be condemned The type of cardiac disease, the functional capacity of the heart and the history of decompensation are factors of importance in the anesthetic management of such surgical patients Such patients should be regarded as cardiac patients who have a surgical disease as a complication, rather than patients with a surgical disease who have a "medical" complication, as is often done

## CORONARY ARTERY DISEASE

In spite of the large number of surgical patients who have sclerosis of the coronary arteries, myocardial infarction and sudden death from this cause on the operating table are, relatively speaking, uncommon Post-operatively such manifestations of coronary artery disease are frequent Some clinicians feel the unwise and promiscuous use of narcotics at this time is a contributory factor Possibly the formation of a thrombus is initiated during operation and the symptoms manifest themselves later In any event when coronary artery disease exists any procedure or anesthetic technique which disturbs blood pressure that is, causes it to rise or to fall is to be avoided Spinal anesthesia is avoided for this reason The so called controlled hypotension is also avoided Anything which precipitates excitement or leads to anoxia during induction is to be avoided For this reason sedation must be carefully selected and never omitted Prolonged stormy inductions, struggling and straining are to be avoided A rapid induction using cyclopropane or basal narcosis with an intravenous short or ultra short acting barbiturate to make the induction uneventful and smooth is indicated Drugs which depress the heart muscle or increase cardiac irritability are not to be used This precludes the use of cyclopropane except for induction Clinical experience has shown that cyclopropane administered for brief periods in the lighter planes does not disturb cardiac rhythm or alter blood pressure significantly It is the continued use of deep cyclopropane anesthesia which may affect the heart adversely Chloroform, trichlorethylene or ethyl

chloride are not to be used when definite evidence of *coronary artery disease* exists Straining from attempting intubation during light anesthesia likewise should be avoided by the anesthetist because it elevates both venous pres sure and blood pressure and initiates reflexes mediated over the autonomic nervous system Epinephrine must not be added to solutions of local anes thetic drugs if regional anesthesia is used in these patients

Myocardial disease which has resulted from a previous infarction is managed *in the same manner* as outlined above

## MYOCARDITIS

The term myocarditis as used in this discussion refers to afflictions of the myocardium resulting from toxic agents or infections such as diphtheria, typhoid or rheumatic fevers, myocardial abscess or subacute bacterial endocarditis When surgery is indicated in these patients, the management of anesthesia differs in no way from that outlined for coronary artery dis ease Drugs which reduce cardiac output by depressing the myocardium are to be avoided as are those which increase cardiac irritability

## VALVULAR DISEASE

The anesthetic management of patients with valvular lesions depends largely on the valve or valves which are involved and the associated changes in function and reserve caused by the lesion Long standing valvular lesions which are slight and without symptoms are usually disregarded When well established valvular disease exists and signs of enlargement and impairment of function are present the anesthetic management differs little if at all from that outlined for patients who have myocardial disease

*Mitral Stenosis* is the commonest serious valvular lesion encountered The more or less fixed cardiac output in well established stenosis may lead to difficulty The possibility of right sided heart failure during surgery must be borne in mind Pulmonary *edema and hemoptysis are possible complica* tions during surgery The dependent position, excitement, or straining during intubation are to be avoided during the induction and maintenance of anes thesia The selection of drugs and techniques differ in no way from that outlined for coronary artery disease "Overindulgence" in blood and fluids is often much more of a problem than is the anesthetic agent

*Mitral insufficiency* is managed in the same way as mitral stenosis Left-sided heart failure may be present or may develop during operation Inasmuch as disease of the mitral valve is often associated with rheumatic fever, the possibility of the co existence of each should be borne in mind

*Stenosis and insufficiency of the tricuspid valve* are rarely encountered in surgical patients The anesthetic management is the same as for disease of the mitral valve When not in failure, the heart rarely gives concern Avoidance of hepatotoxic agents and substances conjugated or excreted by

the liver is a real concern The cyanosis and high venous pressure may be more alarming to the anesthetist than warranted

*Aortic insufficiency* whether rheumatic or luetic in etiology is not to be regarded lightly unless the lesion is dynamically mild—as reflected by an essentially normal diastolic pressure at rest The low diastolic pressure associated with the lesion is of particular importance to the anesthetist Any further lowering of blood pressure may cause coronary insufficiency by reducing coronary blood flow Reductions in peripheral resistance or cardiac output may further curtail coronary flow and cause an insufficient supply of blood Spinal anesthesia, controlled hypotension and deep ether anesthesia should be scrupulously avoided Obviously any increases in the work load of the heart places a strain upon the left ventricle which may precipitate cardiac failure Anoxia, carbon dioxide excess or intubation during light anesthesia are detrimental Epinephrine and other vasoconstrictors are not to be combined with the local anesthetic drug if regional anesthesia is selected Nitrous oxide or ethylene followed by ether or a basal narcosis with thiopental intravenously followed by nitrous oxide or ether may be used

## CONGENITAL DEFECTS OF THE HEART

The anesthetic management of patients with *congenital lesions* of the heart cannot be empirically outlined because of the wide variations and combinations encountered One striking characteristic of congenital heart lesions in infants and children is that the myocardium is frequently not functionally impaired The hearts of such patients are not prone to develop cardiac failure In older subjects when the anomaly has been long standing the myocardial reserve is impaired and cardiac failure may develop during surgery

The most common congenital lesion encountered is the *Tetralogy of Fallot* and its variations Such patients present signs of increased blood volume, increased blood viscosity and reduction in arterial blood oxygen saturation Excitement, apprehension and respiratory dysfunction cause the oxygen saturation to fall still more Any further increase in blood volume or a reduction in oxygen saturation are to be avoided As a rule, basal narcosis with intravenous thiopental followed by cyclopropane induction and ether sequence is the usual choice The use of spinal anesthesia, chloroform, ethyl chloride or trichlorethylene is not advised

Patent ductus arteriosis is occasionally encountered as a complication of a surgical disease When long standing impairment of function exists the anesthetic management of such patients is similar to that for those who have myocardial impairment

## CARDIAC ARRHYTHMIAS

Most arrhythmias encountered in surgical patients are associated with some form of heart disease The anesthetic management depends upon the

nature of disease causing the arrhythmia Arrhythmias of functional origin such as premature beats and sinus arrhythmias, are disregarded Anesthesia is managed in the same manner as if they were not present The most common and serious arrhythmia encountered is auricular fibrillation Inasmuch as this arrhythmia is usually a manifestation of serious cardiac disease and can be caused by a number of clinical conditions, management of anesthesia depends upon the underlying cause

## CARDIAC FAILURE

The management of anesthesia for patients who have well defined cardiac failure is difficult Obviously even the patient in mild failure is a poor surgical risk Whenever possible, surgery should be deferred until the situation improves Regardless of the choice of anesthetic, the possibility of survival is invariably reduced in most instances Whenever possible local anesthesia should be used as it is the least innocuous Epinephrine should not be combined with the local Spinal anesthesia is to be avoided because it adds insult to an obviously decompensated cardiovascular system When general anesthesia is required, inhalation anesthesia is the best Ether with as high an oxygen tension as possible is the best choice A basal of a short or ultra short acting barbiturate is advisable as a preliminary to inhalation anesthesia The non volatile drugs should be used sparingly because they may affect respiration and aggravate the dyspnea and orthopnea Oxygen under positive pressure and phlebotomy may be necessary to combat pulmonary edema should it occur during surgery The anesthetic apparatus may be used for administering the positive pressure Spinal anesthesia has been advocated for patients in failure on the assumption that it causes an internal phlebotomy and allows pooling of the blood in the venous circuit in the extremities This may have a logical basis from the theoretical standpoint but actual clinical practice does not substantiate this contention

## BLOOD VESSELS

### Arteriosclerosis

Arteriosclerosis is so frequently encountered in surgical patients particularly in the older age group that one is surprised if it is not present Unless the disease is widespread, diffuse, long standing and complicated by heart and renal disease, the anesthetic management of such patients presents no difficult problems When generalized arteriosclerosis is present the chief concern is the lack of elasticity of the vessel walls and its effect on blood pressure and vasomotor stability Anesthetic techniques and drugs which cause changes in cardiac output and raise or lower blood pressure are to be avoided Spinal anesthesia is not as well tolerated as general anesthesia Anoxia, $CO_2$ excess and on occasions cyclopropane cause alarming rises of blood pressure Oversedation often causes the other extreme, a fall in blood

pressure Cyclopropane may be used if there is no cardiac involvement Ether preceded by ethylene or nitrous oxide with a basal of thiopental or seco barbital is the best choice When hypotensive states develop the response to vasopressor drugs and fluids is not as one would desire The blood pressure is inclined to fall when anesthesia is deep Overmedication with morphine, avertin or other non volatile drugs causes hypotension from depression of the vasomotor center Cerebral and coronary thrombosis are especially likely during hypotensive episodes

## Aneurysms

Aneurysms particularly of the luetic type present no problem from an anesthetic point of view, unless they encroach upon the trachea and bronchi in which case they give rise to pressure symptoms, dyspnea or cough, or if they encroach upon the recurrent laryngeal nerves giving rise to vocal cord paralysis If aortic insufficiency is present the management is as described under the heading (Page 184) Excitement, carbon dioxide excess, anoxia, straining due to nausea, vomiting, coughing, stormy prolonged inductions, in fact anything which raises blood pressure are to be avoided Ether, cyclopropane, or a basal of an ultra short acting barbiturate combined with nitrous oxide may be used When cough is present it is associated with a tendency towards bronchospasm and laryngospasm Thiopental should then be avoided The use of spinal anesthesia is questionable in these patients and is best avoided whenever possible because of its effects on blood pressure When surgery is being performed on an aneurysm in the lower part of the body surgeons prefer spinal anesthesia The possibility of hemorrhage is to be borne in mind in this selection It is a well established fact that patients under spinal anesthesia do not tolerate any sizable changes in blood volume

*Arteriosclerotic aneurysms* present the same problems and are managed in the same manner as the luetic type

*Arteriovenous fistulas* are shunts from the arterial to the venous side of the vascular system Such a defect places an extra burden on the heart Hypertrophy and signs of cardiac failure are common The selection of anesthesia depends upon the status of the heart If a defect is not a long standing one and cardiac involvement is not pronounced the choice of anesthesia is immaterial Whatever is best to permit the operator to perform the surgery is used. If the heart is involved the anesthetic management is similar to that as described for heart disease A smooth induction is of especial importance

## Hypertension

Essential hypertension uncomplicated by cardiac or renal involvement does not pose any serious problem as regards to choice of anesthesia Drugs or methods which markedly elevate or lower the blood pressure are to be

avoided Ether, nitrous oxide or ethylene without anoxia may be used It is best to avoid excitement and sub oxygenation by use of basal narcosis as an adjunct to anesthesia Cyclopropane may be used, but if the blood pressure rises appreciably, must be combined with or supplemented by ether Spinal anesthesia, particularly high spinal, may cause the blood pressure to fall precipitously When local anesthesia is used for non sedated apprehensive patients excitement causes a further elevation in blood pressure Epinephrine should be omitted from solutions of local anesthetics used for nerve blocking or infiltration Stormy inductions and difficult intubations may cause further elevations in blood pressure Precautions to prevent further elevations or falls in blood pressure are to be observed when hypertension complicates renal disease or hypertension is complicated by renal disease The management of patients with hypertensive cardiac disease is similar to that described for cardiac disease in general Hypertensive patients who have had apoplexy are managed in the same manner as patients who have uncomplicated essential hypertension Avoidance of rises or falls in blood pressure is the important point

## Hypotension

Hypotension encountered in surgical patients has a varied etiology It may be "essential," it may be due to changes in blood volume, it may be neurogenic in origin due to autonomic disturbances or it may be due to a combination of both neurogenic factors and alterations in blood volume Hypotension due to shock, blood loss, absorption of toxic substances and so on must be controlled by proper therapeutic measures or correcting the surgical disease causing it before anesthesia is induced A labile, controllable anesthetic and adequate oxygenation is desirable for a patient in shock Non volatile drugs are avoided because they are slowly detoxified They often cause further decreases in blood pressure, respiratory depression, and prolonged somnolence in the postoperative period For patients in shock due to decreases in blood volume, cyclopropane, ethylene or nitrous oxide (without anoxia) may be used Attempts should be made to overcome the hypotension and its cause

Local infiltration or nerve blocks may be used for minor procedures or in severe shock states in which surgery cannot be deferred Ether and chloroform, anoxia, carbon dioxide excess and heat are avoided because of the vasodilating effect or alterations in capillary permeability or both Neurogenic shock, after being corrected by vasoconstrictors or fluids or both, is best handled with cyclopropane, ethylene or nitrous oxide ether which is adequate in most instances Spinal anesthesia and muscle relaxants are avoided in all hypotensive states irrespective of cause Narcotics, if used, are best administered intravenously Overdosage may occur from the cumulative effect when the circulation improves, particularly if several doses have been administered subcutaneously

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content and its influence on oxygen capacity Drugs which are effective at high partial pressures, such as nitrous oxide, are hazardous when administered in the presence of anemia because of the possibility of asphyxia through technical error Cyanosis, one of the warning signs of anoxia, does not appear until severe degrees of sub oxygenation are present It is a matter of common knowledge that the appearance and intensity of cyanosis depends upon a number of factors, notably the amount of reduced hemoglobin present per unit volume of blood at the moment, the thickness of the skin, the amount of pigment in the skin, the caliber of the blood vessels in the skin and the visual acuity of the observer Cyanosis is not a reliable sign of the degree of sub-oxygenation

Concentrations of nitrous oxide or ethylene exceeding 50 or 60 per cent delivered to the inhaler at less than minute volume exchange may be hazardous to anemic patients Cyclopropane permits adequate oxygenation, is labile and quickly eliminated It is the most desirable choice for these subjects Ether skillfully used is safe also Spinal anesthesia prolongs circulation time In the face of the hypotension which develops local tissue anoxia may result Therefore its use is not advised when anemia of any notable degree is present Non volatile drugs cause hypoventilation which may lead to sub oxygenation and carbon dioxide retention They are therefore undesirable when anemia is present There is some question concerning the use of muscle relaxants in anemic patients The hydrolysis of succinyl choline may be delayed if the disease which has given rise to the anemia has given rise to abnormally low cholinesterase levels

The sickling effect in vitro of erythrocytes of patients with sickle cell anemia caused by lowering the oxygen tension is well known to most physicians The possibility of intravascular sickling, therefore, must be borne in mind during general anesthesia Nitrous oxide or ethylene may be undesirable choices because anoxia is an ever present possibility during its administration No evidence exists that any of the currently used drugs, either volatile or non volatile, causes intravascular sickling, however Obviously technical manipulations of anesthesia predisposing to inadequate ventilation are to be avoided

## Blood Dyscrasias

Blood dyscrasias particularly those characterized by a hemorrhagic tendency cause the anesthetist some concern Instrumentation of any sort such as introduction of airways, laryngoscopy, endotracheal intubation may cause trauma of the mucous membranes and initiate bleeding from the nose, pharynx, trachea or from the site of a needle puncture if intravenous or spinal anesthesia is used In this type case the fewer the manipulations the better However if the clotting mechanism is not disturbed and there is no tendency towards bleeding the choice of anesthesia differs in no way from that de

Essential hypotension is managed in the same manner as hypotension due to shock, hemorrhage and other causes Spinal anesthesia lowers blood pressure further Such hypotension is not readily corrected by vasopressors Cyclopropane, ether, ethylene or nitrous oxide may be used This can often be controlled preoperatively by desoxycorticosterone and sodium chloride The barbiturates intravenously, avertin or oversedation with narcotics cause vasomotor depression and may further lower blood pressure

## BLOOD

Anesthetics do not affect the morphology of the blood cells in any clinically significant manner They do, however, cause changes in blood volume Alterations of capillary permeability, disturbances in absorption and elimination of water, disturbances of osmotic pressure relationships and alterations in size of the spleen influence blood volume and the total hemoglobin content per unit volume of blood Decreases in blood volume are manifested by a hemoconcentration, an increase in hematocrit and hemoglobin readings Decreases in hematocrit usually indicate that the blood volume is reduced due to loss of plasma but they are not necessarily an index of the actual blood volume Changes in blood volume vary with the drug used, the duration of anesthesia, the status of the patient prior to anesthesia, effect of trauma during operation and other variable factors The manner in which changes in blood volume resulting from anesthesia further influence the course of surgery is not known On the whole they appear to be of little significance in average situations

Anesthetics do not affect the oxygen carrying power of the erythrocytes None of the currently used drugs enters into combination with hemoglobin or other cellular constituents The clotting and bleeding times are not appreciably influenced by anesthetics Minor variations caused by individual agents are not significant clinically The clotting mechanism is not influenced by anesthetics The supposed increased bleeding of which surgeons complain during operation is due to oozing caused by local dilatation of the arterioles and capillaries either by the anesthetic, carbon dioxide retention and other factors which affect metabolism They are not due to disturbances of the blood clotting mechanism Bleeding and clotting times are normal during anesthesia with the currently used drugs Prothrombin time is influenced little, if at all, by anesthetics during operation Chloroform is the most important of the drugs which prolong prothrombin time significantly During spinal, nerve block and infiltration anesthesia there is little or no change in bleeding or clotting time

### The Anemias

Irrespective of the type and causes of an existing anemia the prime consideration as far as anesthesia and surgery is concerned is total hemoglobin

leucocytosis is not known, but it does not operate in patients who have agranulocytosis

REFERENCES

BELINKOFF S Choice of anesthesia in cardiac disease *Anesthesiology 7* 268-275, 1946

BLALOCK, A. Cardiac output during ether anesthesia. *Arch Surg 14* 732, 1927

DRIPPS R. D The immediate decrease in blood pressure seen at the conclusion of cyclopropane anesthesia. *Anesthesiology 8* 15–31 1947

EDITORIAL The cardiac patient as a surgical risk. *South Gen Pract 118* 49 1953

FOLLIS R. Coronary arteries in relation to sudden death during anesthesia. *Bull Johns Hopkins Hosp LXVII* 211–217 1940

GARCIA J E MIDDLETON S L. and ANDERSON A. E. The cardiac patient as a surgical risk *New Orleans M & S J 104* 715 1952

JOHNSTONE M. The cardiology of anesthesia. *Anesth & Analg 31* 325 1952

MEEK W J HATHAWAY H. R. and ORTH O S The effects of ether chloroform and cyclopropane on cardiac automaticity *J Pharmacol & Exper Therap*, *61* 240 1937

MORRIS L. E. and BRUNO H. The effects of procaine amide on cardiac irregularities during cyclopropane anesthesia. *Anesthesiology 12* 328 1951

MUSHIN W W *Anesthesia for the Poor Risk* Springfield Thomas 1948

PENDER, J W and ESSEX, H. E. A study of traumatic shock under certain anesthetics. *Anesthesiology 4* 247–252 1943

PRICE H. L CONNER, E. H. DRIPPS R. D Concerning the increase in central venous and arterial blood pressure during cyclopropane anesthesia in man. *Anesthesiology 14* 1–9 1953

REID C Anesthesia in relation to cardiac disease *Anesthesiology 2* 161 1941

SMITH H. W ROVENSTINE, E. A. GOLDRING W *et al* The effects of spinal anesthesia on the circulation in normal unoperated man with reference to autonomy of the arterioles and especially those of the renal circulation. *J Clin. Investigation 18* 319 1939

SMITH R. M. Circulatory factors affecting anesthesia and surgery for congenital heart disease. *Anesthesiology 13* 38-50, 1952

TAYLOR, L B Cyclopropane anesthesia. *Anesthesiology 2* 641 1941

scribed for the anemias When the erythrocyte count, hematocrit or hemo globin are normal there is little to cause concern in dealing with blood dyscrasias, except sickle cell anemia where, theoretically at least, anoxia and $CO_2$ excess are to be avoided

Polycythemia whether primary or secondary presents no particular problem as far as selection of anesthesia is concerned These patients may appear cyanotic but this need be of no concern because the oxygen capacity is greater than normal and the oxygen content of arterial blood is normal or better than normal The dilated vessels commonly observed predispose to increased bleeding The possibility of thrombus formation must be borne in mind This is of more concern to the surgeon than the anesthetist but it must also be borne in mind by the anesthetist, however

## Leukemia

Patients with leukemia occasionally require surgery The items of interest to the anesthetist in patients who have leukemia are the anemia, the fever, the excess lymphoid tissue, the asthenia, the altered metabolic rate and the bleed ing tendency Collections of lymphoid tissue in the pharynx, in the fauces, around the epiglottis and larynx obstruct the airway and not only cause ob struction to respiration but also often make intubation difficult Sometimes oropharyngeal infection is present Enlarged lymph glands in the medias tinum may compress the trachea and bronchi and cause dyspnea and obstruction The basal metabolic rate is elevated but these subjects are non resistant and quickly respond to both volatile and non volatile anesthetics Cyclopropane, nitrous oxide or ethylene with ether, or local infiltration and nerve blocks are well tolerated by patients with leukemia Non volatile drugs which depress respiration and cause hypoventilation are avoided because of the impaired oxygen carrying power due to the anemia Spinal anesthesia is likewise avoided for the same reason

In the absence of anemia if the patient is in good physical condition, spinal anesthesia may be used, but in chronically ill patients spinal anesthesia is to be avoided, generally

## Lymphomas

Patients with Hodgkin's disease, lymphosarcoma and other malignant lymphomas present basically the same problems as those having leukemia Anemia, enlarged glands, excess lymphoid tissue, oropharyngeal sepsis and fever are items of interest.

Patients with agranulocytosis occasionally require surgery for incisions and drainage or for some septic condition The deficiency in leukocytes has no bearing on anesthesia because of the formation or morphology of white cells It is known that after surgery the leukocytes increase in number, that is, in individuals whose bone narrow is normal The mechanism causing the

hydrocarbons. The vapors of volatile liquids cause exaggerated respiratory movements which further enhance this dissemination. The non volatile drugs are not without drawbacks. The ultra short acting barbiturates particularly the thiobarbiturates are laryngospasmogenic and bronchospasmogenic. The mucoid or purulent secretions which are present *in the respiratory tract in* most acute and chronic infections often give rise to laryngeal or bronchial spasm, coughing *and even sneezing because these reflexes not only are not* obtunded but are even exaggerated by these drugs. In addition they invariably cause hypoventilation which is one of the predisposing causes of atelectasis. Avertin is objectionable from the standpoint of hypoventilation.

The best selection when infection is present in the upper respiratory tract is some form of regional anesthesia. High spinal anesthesia is best avoided because of the hypoventilation. Low spinal anesthesia may be used. Inhalation anesthesia with cyclopropane, ethylene or nitrous oxide are the best choices when local, spinal or regional anesthesia cannot be used. A basal of a short-acting or ultra short acting barbiturate may be combined with nitrous oxide but this is a less desirable choice. Occasionally one must choose between ether and another drug—*as for example cyclopropane when cardiac disease* is present. The question then is which is the lesser of two evils. The proper antimicrobial therapy before and after surgery, immediate and repeated hyperventilation and forced coughing postoperatively, restriction of narcotics (use blocks), and expectorants reduce the danger in acute respiratory infections considerably.

## CHRONIC UPPER RESPIRATORY INFECTIONS

Chronic infections of the upper respiratory passages are frequently associated with post nasal drip due to allergic disease or chronic sinusitis. The management of anesthesia when this type of infection exists differs in no way from that of acute as to the upper respiratory infection. The possibility of "spread" of infection, however, is less in chronic infections than acute. *Aggravation does not appear to occur as readily or frequently.* In long standing chronic illness from these diseases there is little point in deferring surgery. In instances in which the symptoms are not due to bacterial infection but to allergic responses, such as hay fever, allergic rhinitis, bacterial allergy and such related entities the difficulties center about those caused by secretions. These initiate spasm which causes respiratory obstruction. Premedication with a combination of an anticholinergic drug (atropine) and an antihistaminic drug is desirable when an allergy is present which causes symptoms referable to the respiratory system. Anesthesia for *chronic bronchitis* is managed *in the same manner* as upper chronic respiratory tract infections. Detergents (such as alevaire) probably help in chronic bronchitis if cilia have not been destroyed.

## XIX

# DISEASES OF RESPIRATORY SYSTEM

Anesthetics affect the respiratory system in a number of ways (1) by stimulating the flow of secretions from the mucous and salivary glands, (2) by causing hypoventilation leading to sub oxygenation and carbon dioxide retention, (3) by decreasing ciliary activity, (4) by stimulating re flexes such as the laryngeal, tracheal, and bronchial, and (5) by acting as primary chemical mucosal irritants

There is no evidence that the currently used inhalation anesthetics cause any histological change in the tissues of the respiratory system Likewise there is no evidence that these drugs affect the diseased lung Pathologic conditions involving the lung fall into two major categories, as far as anesthesia is concerned (1) Those which interfere with ventilation such as fibrosis, neoplasms or degenerative diseases (emphysema) (2) Those which interfere with respiration Secretions, tumor masses, spasm, interstitial fibrosis and pulmonary vascular disease are included in this category

## ACUTE RESPIRATORY INFECTIONS

It is taught, and with good reason, that general anesthesia is to be avoided in acute infections of the respiratory tract particularly the upper portions Statistical data indicate that the incidence of postoperative pulmonary complications is greater when surgery is complicated by acute respiratory infections This observation applies to all types of anesthesia, inhalation, in travenous or regional or combinations of these *There is a deep seated erroneous impression in the minds of many clinicians that as long as an anesthetic is not inhaled no undesirable postoperative sequelae of a respira tory nature result* The logical course to follow is to defer surgery when an acute respiratory infection exists

When an acute respiratory infection is present, and one proceeds with an elective operation, the act should constitute malpractice When surgery is urgent and the operation cannot be deferred regional anesthesia is pre ferred to general When general anesthesia is indicated the gases are pre ferred to the volatile liquids because they cause less salivation and mucous formation Evidence exists that the flora of the upper respiratory tract mixes with that of the lower by dissemination of the secretions This dissemina tion is enhanced by the loss of ciliary activity The volatile liquids stimulate secretory activity more than the gases The latter are preferred when inhala tion anesthesia is selected Ethers appear to do so more than halogenated

biturates The ever present secretions often initiate vexsome bronchial and laryngeal spasm Other non volatile drugs such as avertin, or morphine or morphine substitutes may cause an undesirable respiratory depression There is no objection to the use of the muscle relaxants provided adequate ventilation is maintained

## TUBERCULOSIS

The problem of anesthetizing patients with pulmonary tuberculosis arises frequently Tuberculous patients frequently develop diseases requiring both elective and emergency surgery The status of tuberculous patients varies considerably from one subject to the next Some have minimal lesions and are, generally speaking, in good physical condition In other cases the disease has been long standing and destruction of lung tissue has caused a reduction in ventilating surface in the lung Secretions, adequate gaseous exchange and prevention of dissemination of infection are the chief problems encountered Fever, weight loss and anemia are often factors to be considered also

In general, choice and management of anesthesia is similar to that outlined for suppurative diseases of the lung Regional anesthesia is preferred whenever it can be used When general anesthesia is required the gases, cyclo propane ethylene or nitrous oxide, may be used without fear The thiobarbiturates are spasmogenic and cause respiratory depression It is best to avoid them as well as other non volatile drugs which depress respiration It has been taught, and is still taught by many, that ether aggravates pulmonary tuberculosis There is no proof of this Most clinicians feel that a quiescent lesion may become active because the general state of the patient is altered by surgery and that the resistance is lowered, irrespective of the anesthetic drug used The only possible influence ether, chloroform, vinyl ether or other volatile drugs have upon a tuberculous lung, is the dissemina tion of infection by secretions That this occurs has never been proved How ever, ether has been and is used for pulmonary resections and thoracoplasty with excellent results

## MYCOTIC DISEASES OF THE LUNG

The problems and anesthetic management of patients who have actinomy cosis and blastomycosis and other mycotic lesions are similar to those outlined for patients who have pulmonary tuberculosis

## PNEUMOCONIOSES

Silicosis, anthracosis, asbestosis and similar pneumoconioses are characterized by varying degrees of interstitial fibrosis of the lung and emphysema The reduction in pulmonary ventilating surface and secretions are the two factors of concern to the anesthetist The anesthetic management in general

## ACUTE TRACHEOBRONCHITIS AND PNEUMONITIS

The management of anesthesia for patients who have tracheobronchitis complicating a surgical disease differs in no way from those for patients who have acute respiratory infections Pneumonitis whether lobar, lobular or interstitial, all present the same problem as far as anesthesia is concerned namely those caused by fever, sepsis, exudates and inadequate ventilating surface Diffuse interstitial and lobular pneumonia give more anoxia and $CO_2$ accumulaton than other types of pneumonitis Carbon dioxide retention and anoxia are of the utmost concern particularly in the diffuse interstitial and lobular types of infections Obviously any anesthetic technique or drug which exaggerates these symptoms and manifestations is to be avoided Ether increases secretions and causes exaggerated breathing both of which help disseminate infection The halogenated hydrocarbons do likewise but to a lesser degree Non volatile substances particularly the ultra short acting and short acting barbiturates are spasmogenic and cause hypoventilation They are not, therefore, suited for anesthesia when these diseases are present Secretions in the respiratory tract may initiate bronchial or laryngeal spasm Avertin depresses respiration and thus adds further to any existing anoxia and carbon dioxide retention Ethylene and nitrous oxide do not stimulate flow of secretions or cause exaggerated breathing, and would seem desirable However, in the presence of fever the safe limits of sub oxygenation may be exceeded with these two gases, particularly when anoxia due to the disease is already present Cyclopropane is non irritating, allows adequately oxygenation, is labile, rapidly eliminated and probably is the most satisfactory choice for these conditions Regional block, spinal anesthesia and local infiltration are the most desirable when they can be used but this is not always feasible The importance of preoperative and postoperative therapeutic bronchoscopy cannot be overemphasized in these cases

## SUPPURATIVE DISEASES

Suppurative diseases of the lungs encountered in surgical patients include bronchiectasis, lung abscess, gangrene or infected cysts Patients so afflicted are often difficult to anesthetize using general anesthesia Fever, cachexia, anemia and all the manifestations of long standing sepsis are the rule rather than the exception In addition these patients frequently have a hyperactive cough reflex which is troublesome throughout operation Dyspnea, orthopnea, cyanosis and other manifestations of inadequate ventilation may be present Spasmogenic drugs are avoided because they further exaggerate the cough reflexes in the tracheobronchial tree Spinal or local infiltration or nerve blocks are preferred When general anesthesia must be used, cyclopropane is the best choice When light anesthesia with no relaxation is desired, ethylene or nitrous oxide are good choices A basal of thiopental is not always satisfactory because of the spasmogenic nature of the thiobar-

causing obstruction until an endotracheal catheter is introduced The presence of the neoplasm often causes hyperactive tracheobronchial reflexes in some patients and bronchial spasm results when inhalation anesthetics are administered, particularly ether The thiobarbiturates likewise cause spasm

## DEGENERATIVE DISEASES OF THE LUNG

The most important disease listed in this category is chronic obstructive emphysema The diminished pulmonary reserve, fixation of the chest wall, increased functional residual air volume, high pulmonary carbon dioxide tension, and the associated cardiac disease are all factors which render the management of anesthesia in these subjects difficult The cardiovascular disease particularly complicates the management of anesthesia considerably Actually there is no wholly satisfactory method of anesthetizing patients with emphysema The inhalation anesthetics are unsatisfactory because the diminished alveolar surface and the large functional residual air volume prevent adequate mixing and diffusion of the anesthetic gases from the alveoli into the blood and vice versa Non volatile drugs cause respiratory depression which likewise is undesirable The hypoventilation enhances the respiratory acidosis which is already present High spinal anesthesia decreases pulmonary ventilation and is therefore objectionable from this standpoint Low spinal anesthesia is satisfactory whenever it may be used Local anesthesia may be used for minor surgery General anesthesia is the best choice for major surgery A combination of cyclopropane and ether is the most satisfactory Muscle relaxants often cause depression of respiration and hypoventilation and are best avoided Patients with a high arterial carbon dioxide tension or respiratory acidosis should not undergo surgery without several weeks of graded oxygen therapy and mechanical hyperventilation if this is possible If surgery is not elective, then preoperative and postoperative mechanical ventilation should be planned

## PULMONARY EMBOLISM AND INFARCTION

Occasionally pulmonary emboli complicate a surgical disease and urgent surgery is required in a patient with this complication Surgery should be deferred whenever possible The management of these patients depends upon the extent of the pulmonary infarction and the condition of the patient If the patient is in shock and has respiratory distress surgery should be deferred until such shock is overcome Apprehension and excitement must be avoided In general it is best to avoid the use of inhalation anesthetics Wherever possible local anesthesia or nerve blocks combined with sedation should be used If general anesthesia must be used attempts at a rapid induction must be made Cyclopropane with a high oxygen concentration is undoubtedly the best choice Ether may be added but it causes exaggerated breathing and is best avoided *Nitrous oxide, ethylene, or either of these*

differs little if at all from that outlined for pulmonary tuberculosis, except in advanced cases, in which the problems of ventilation take on a serious aspect

## BRONCHIAL ASTHMA

In asthmatic patients, spasm, secretions, and edema of the bronchi give rise to obstructive dyspnea Surgery should be deferred if the patient has an asthmatic episode Asthmatic patients free from an attack present no special problem if there is no pulmonary infection, chronic emphysema or bronchitis complicating the condition There is no objection to the use of an inhalation anesthetic Nitrous oxide or ethylene for induction followed by ether is preferred because the gases are non irritating and ether is a bronchial dilator Ethylene and nitrous oxide do not exert any notable action on the bronchi, being neither dilators nor constrictors When ether is used, it should be administered slowly to avoid initiating cough and spasm Once the blood concentration necessary for surgical anesthesia has been attained the ether acts as a bronchial dilator Regional anesthesia, if the patient is not allergic to local anesthetic agents, including spinal, may be and should be used when ever possible Chloroform, vinyl ether and ethyl chloride also are bronchial dilators Ethyl chloride however is reputed to cause stridor and to initiate spasm even though it is known to act as a bronchodilator The thiobar biturates and the ultra short acting barbiturates induce bronchial spasm in normal individuals let alone asthmatics, and are therefore avoided Some are sensitive to them Cyclopropane behaves like the thiobarbiturates but to a lesser extent Ether may be added to cyclopropane if it is used and broncho spasm develops The narcotics may cause broncho constriction It is advis *able to ascertain before surgery to which drugs the patient responds ad* versely and be guided accordingly in prescribing preanesthetic medication and postoperative sedation

"Cardiac asthma" presents problems which differ radically from those of asthma due to allergy The anesthetic management for these subjects is similar to that outlined for cardiac disease In addition one must avoid spasmogenic drugs The use of aminophylline and similar bronchial dilators is advised in these cases whenever indicated

## NEOPLASMS OF THE LUNG

The most commonly encountered neoplasms of the lung are carcinoma of the bronchi and of the lung parenchyma *Unless there is extension of the* neoplasm or the new growth is complicated by suppuration the anesthetic management of these patients offers no problem as a rule If an abscess is present, then the management is identical to that described under suppura tive diseases of the lung It is not unusual for these patients to have vocal cord paralysis particularly on the left side This troubles the anesthetist by

## REFERENCES

Beecher, H. K. *Anesthesia for Thoracic Surgery* Springfield Thomas 1952

Beecher H. K., Adams R. Ether anesthesia in the presence of pulmonary tuberculosis *J.A.M.A.*, *118* 1204 1942

Beecher H. K. Bennett H S and Bassett, D L Circulatory effects of increased pressure in the airway *Anesthesiology* *4* 612 1943

Burstein, C. L. Respiratory derangements during anesthesia. *New York State J Med*, *42* 1638 1942

Coryllos P and Birnbaum G Studies in pulmonary gas absorption and bronchial obstruction *Am J M Sc* *183* 327, 1932

Gillespie N A. and Conroy W A. Endotracheal anesthesia the relation of nasal tracheal and oral tracheal intubation to respiratory morbidity *Anesthesiology* *2* 28 1941

Green B A. and Berkowitz S The Pre anesthetic induced cough as a method of diagnosis of preoperative bronchitis *Ann. Int Med* *18* 72 1952

Mushin W W *Anesthesia for the Poor Risk* Springfield, Thomas 1948

Nosworthy M D Anesthesia in chest surgery with special reference to controlled respiration and cyclopropane. *Proc Roy Soc Med*, *34* 479 1941

Saklad M Grading of patients for surgical procedures *Anesthesiology* *2* 281 1943

Schmidt C The influence of cerebral blood flow on respiration *Am J Physiol* *84* 202 1928.

Schmidt C. F Carotid sinus reflexes to the respiratory center *Am J Physiol* *102* 94 1942

Slocum H. C. Hoeflich E. A and Allen C R. Circulatory and respiratory distress from extreme position on the operating table. *Surg Gynec & Obst* *84* 1051 1947

gases followed by ether may lead to anoxia, struggling or excitement Large doses of atropine have been suggested preoperatively to reduce vagal reflexes Intravenous thiobarbiturates may be used for a rapid induction but the possibility of spasm must not be overlooked and may make the choice undesirable

## DISEASES OF THE PLEURA

Fibrinous pleurisy without effusion usually presents no problem from the standpoint of anesthesia Inasmuch as this disease is often a complication of disease of the lung parenchyma itself anesthetic drugs which cause exaggerated breathing or any technique of anesthesia which causes hypoventilation are to be avoided For this reason ethylene or nitrous oxide with adequate oxygenation or cyclopropane are preferred When these are contraindicated thiopental with nitrous oxide may be used Spinal anesthesia or local anesthesia is desirable when it can be used and inhalation anesthesia cannot Ether, vinyl ether, chloroform, and ethyl chloride cause exaggerated breathing and secretions

Pleurisy with effusion presents a different problem, however There is usually encroachment of the fluid collection upon the lung parenchyma with a diminution in ventilating surface Pulmonary reserve is diminished More often than not the pleurisy follows a pulmonary infection Dyspnea, fever, cough and other symptoms of respiratory tract infection are present When there is no cause ascribed for the pleurisy, as is often the case, tuberculosis must be suspected These patients are then managed in the same manner as patients who have pulmonary tuberculosis Local anesthesia or regional anesthesia are preferred whenever they can be used Where general anesthesia is to be used cyclopropane is the ideal choice The combination of thiopental and nitrous oxide may depress respiration and are, as a rule, best avoided Ether is a less desirable choice but may be used when other drugs cannot Avertin depresses respiration There is no objection to the muscle relaxants When indicated, reduction of the effusion by thoracentesis should be done preoperatively and repeated if there is a reaccumulation of fluid postoperatively

Acute empyema and hydrothorax are managed in the same manner as pleurisy with effusion Patients with chronic empyema, usually the result of inadequate drainage of acute empyema, may have bronchial or bronchopleural fistulae which give considerable difficulty to the anesthetist Anesthesia is managed in the same way as for patients with acute empyema In bronchopleuro-cutaneous fistulae, if inhalation anesthesia is used, there is a rapid loss of gases and vapors through the opening unless an attempt is made to close the opening

to mechanical restrictions on respiratory movements The respiratory excursions are decreased particularly when the patient is in the prone or lateral position The obese patient is more susceptible to circulatory derangements from positional changes than the thin, slender person The obese patient is not a good subject for nerve blocks because the landmarks are obliterated by the adipose and subcutaneous tissues Degenerative, metabolic, cardio vascular and renal disease are more frequently encountered in the obese patient These complicate the management of anesthesia

If the patient presents complications other than the obesity, the most important consideration, if general anesthesia is to be used, is maintaining an airway and adequate ventilation Spinal anesthesia may be technically more difficult to induce due to obliteration of landmarks and the depth of the vertebrae below the skin "High spinal" anesthesia is often not well tolerated by these subjects because they develop a hypotension "Low spinal" anes thesia is usually satisfactory and preferred because it obviates the many technical difficulties of general anesthesia Reduced hepatic function may be greater following anesthesia in the obese

## EMACIATION, CACHEXIA, STARVATION

Patients who are cachectic are so as a result of some disease entity which impedes nutrition Gastro intestinal lesions, neoplastic disease, mental disease, endocrine disturbances, drug addiction or some such underlying cause may be responsible for the patient's poor state Such patients are "non resistant" to central nervous system depressants They appear to be "sensitive" to drugs, requiring much less than ordinary quantities Non volatile central nervous system depressant should be used with extreme caution because the rate of detoxification may be slow The metabolic rate is reduced, often far below the accepted normal Occasionally, the exception to the rule is encountered and a resistant patient is seen who is difficult to anesthetize

Infiltration or nerve block is the desirable choice of anesthesia for such subjects Cyclopropane, nitrous oxide or ethylene followed by ether may be used Anesthetics which tend to lower the blood pressure should not be used Muscle relaxants should be used with caution particularly succinyl choline Serum cholinesterase may be reduced to abnormally low levels in cachexia Hepatitis due to chloroform and other halogenated hydrocarbons more frequently ensue in starved subjects than in the well fed Glucose or proteins should be given preoperatively Endocrine disturbances causing cachexia merit special consideration These are discussed later on (Chap XXV)

## VITAMIN DEFICIENCIES

No well defined relationship between vitamin deficiencies, particularly when subclinical, and anesthesia has been established When due to severe

## XX

# METABOLIC DISEASES

Anesthetics may cause far reaching disturbances of metabolic processes Acid base balance, carbohydrate metabolism, liver function, and renal function are all altered in some degree by anesthetics Therefore diseases of the liver, kidney and those characterized by disturbance in metabolism merit special consideration

## DIABETES

The greatest concern from an anesthetic standpoint in the management of diabetic patients requiring surgery is the possibility of acidosis The control of blood sugar is of less importance In the pre insulin days the administration of ether to a diabetic patient was tantamount to signing the death certificate for that patient Disturbances in acid base balance caused by ether are of little consequence in normal persons Uncontrollable acidosis invariably results in diabetics Ether causes glycogenolysis and an elevated blood sugar in all subjects but more so in the diabetic Then also the diabetic presents other problems of concern to the anesthetist Many are obese, have arteriosclerosis, pyogenic infections, cardiac disease and hypertension, all of which complicate anesthesia further *Any anesthetic may be administered* to a properly controlled diabetic who is free of other diseases or abnormalities provided the patient is closely observed after surgery Regional anesthesia disturbs the diabetic patient least Spinal anesthesia is satisfactory in most respects

There is objection to the infiltration techniques because the reparative processes of the tissues are often impaired Epinephrine must not be combined with local anesthetic drugs when regional anesthesia is selected especially for surgery of the extremities Cyclopropane, ethylene, nitrous oxide without anoxia cause no disturbances of any consequence in carbohydrate metabolism or acid base balance Vinyl ether and analgesia with trichlor ethylene cause some slight but not significant changes The non volatile drugs such as thiopental and avertin depress respiration and favor respiratory acidosis Morphine may also enhance acidosis in a severe diabetic No contraindication appears to exist to the use of muscle relaxants as adjuncts to anesthesia for diabetics

## OBESITY

The obese patient is a poor surgical risk from the standpoint of anesthesia Comparatively speaking the obese individual is in most instances difficult to anesthetize Maintaining the airway is accomplished with difficulty unless an endotracheal catheter is used Even then ventilation may be inadequate due

to mechanical restrictions on respiratory movements The respiratory excursions are decreased particularly when the patient is in the prone or lateral position The obese patient is more susceptible to circulatory derangements from positional changes than the thin, slender person The obese patient is not a good subject for nerve blocks because the landmarks are obliterated by the adipose and subcutaneous tissues Degenerative, metabolic, cardiovascular and renal disease are more frequently encountered in the obese patient These complicate the management of anesthesia

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nutritional disturbances and emaciation and cachexia exists, the problems are those which have just been mentioned Spinal anesthesia is best avoided when neurological complications are present due to the deficiency Such lesions are most commonly associated with thiamine deficiency Occasionally this deficiency is encountered in alcohol addicts Preoperative preparation with vitamins is indicated whenever a deficiency exists or a subclinical one is suspected

REFERENCES

GAEBARD J and G *et al* The effect of ether anesthesia upon alveolar ventilation and acid base balance in man *Ann Surg* *136* 680 1952

MOORE F D *Metabolic Response to Surgery* Springfield, Thomas 1952

NASH J *Surgical Physiology* 2nd Ed Springfield Thomas, 1953

STORMONT H. R. HATHAWAY F E., SHIDEMAN F E and SEEVERS M H. The acid base balance during cyclopropane anesthesia *Anesthesiology* *3* 369–378 1942

# XXI

# GASTRO-INTESTINAL SYSTEM

## STOMACH AND INTESTINES

Diseases of the grastro intestinal tract offer no particular problems from the standpoint of anesthesia unless the condition present is accompanied by dilatation of the stomach with retention, obstruction or has led to weight loss, cachexia, vitamin deficiency and other metabolic derangements The possibility of regurgitation or aspiration in obstructive lesions is the chief concern of the anesthetist when gastro intestinal lesions are present Pre operative gastric intubation and aspiration are indicated when retention or distention are present Rectally administered drugs are contraindicated in colonic and rectal diseases

## PANCREAS

Diseases of the pancreas are included with gastro intestinal lesions be cause they lead to or are manifested by jaundice, weight loss, disturbances in carbohydrate and fat metabolism Anesthesia for patients with pancreatic disease is considered in the light of these metabolic alterations Patients with acute pancreatitis invariably are severely ill and are usually poor surgi cal risks Hypotension occurs often precipitously when anesthesia is induced particularly when spinal anesthesia is used The fall in blood pressure does not respond to the usual therapeutic measures such as vasopressors and fluids

## LIVER

The medical literature is replete with discussions on the effects of anes- thesia upon liver function Many studies have been reported on this im portant topic but, in spite of it all, much of the information available merely supplies a theoretical rather than a practical guide to the manage ment of anesthesia for patients who have liver disease and impaired liver function Most of the data are based on tests of a single or a few of the numerous liver functions The most widely utilized and simplest test which introduces the fewest variables as far as anesthesia is concerned is the bromsulfalein excretion test Measurement of hyperglycemic effects, bile and bile salt excretion, hippuric acid synthesis, cephalin flocculation have been used but are less reliable In most studies tests have been performed on normal livers Little data is available on the effects of anesthesia on diseased livers In general, it is agreed that cyclopropane, ethylene and nitrous oxide have little or no significant influence on most liver functions

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Severe hypotension leading to irreversible circulatory collapse is a strong possibility under these circumstances

## Fibrosis and Degeneration of the Liver

Although fibrosis of the liver develops from a number of causative mechanisms and results in varied histological pictures, functionally the problems concerning anesthesia are the same The end result of the pathologic process is the same, namely a decrease in the mass of liver tissue and subsequent hepatic insufficiency Gastro intestinal symptoms such as nausea, vomiting, diarrhea with dehydration may be present The lowered serum proteins and venous engorgement give rise to ascites and edema Anemia is common A hemorrhagic tendency is present due to reduced platelets, fibrinogen and prothrombin Bleeding from esophageal varices may be present Patients with such symptoms of far advanced hepatic fibrosis are obviously poor surgical risks

Patients with ascites do not tolerate spinal anesthesia, therefore, this choice is not open to the anesthetist The anemia precludes the use of nitrous oxide or ethylene unless anoxia can be avoided The non volatile drugs may not be detoxified in a normal manner They may cause prolonged somnolence and likewise should be avoided Cyclopropane is one of the best choices because it is labile, rapidly eliminated and disturbs liver function least of the major anesthetics Ether causes some impairment in liver function and is therefore avoided When used some patients may develop hepatic coma and death Barbiturate anesthesia—or even opening the abdomen under local anesthesia have been known to do likewise Regional or local infiltration is probably the best where applicable When local anesthesia is used it must be remembered that the drug may be detoxified slowly and toxic reactions may occur when the usual quantities are employed

## Abscesses of the Liver

Usually liver abscesses are amebic or bacterial in origin Even though extensive usually enough liver tissue remains so that severe hepatic insufficiency is uncommon More often than not the choice is predicated upon the presence of fever, sepsis, weight loss, cachexia and other systemic derangements rather than liver insufficiency The choice is whatever is best to facilitate completion of the surgery Wherever possible local anesthesia is used Otherwise cyclopropane is selected Non volatile drugs are avoided on the presumption that some hepatic insufficiency exists

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Clinical experience seems to indicate that anesthesia per se when conducted with the currently used drugs does not seriously influence the course of liver disease Other factors such as blood loss, surgical trauma, operating time and so on appear to play a greater role Patients showing the greatest reduction in function and the slowest return to preoperative status are those who have serious impairment prior to surgery and those undergoing long, formidable operations If a muscle relaxant is required in conjunction with anesthesia succinyl choline is the best of the currently available drugs because of its rapid hydrolysis by cholinesterase However, even this drug must *be administered cautiously and with extreme care because of the possibility* of a low serum cholinesterase level which may accompany liver diseases and other chronic illnesses The exact fate of other muscle relaxants is not known It is presumed that they are partly detoxified by the liver, the re*mainder being eliminated unchanged by the kidney In the presence of* liver or renal disease, prolonged relaxation, respiratory paralysis, and hypotension may occur due to the slow rate of elimination

## Jaundice

When jaundice complicates a surgical disease the usual inference is that some hepatic insufficiency exists While this may not necessarily be so, particularly in the hemolytic diseases and when the jaundice has been of brief duration, it is perhaps wise to follow this course and manage anesthesia for such patients in the same manner as one would when dealing with hepatic insufficiency without jaundice Non volatile drugs are best avoided or used with extreme caution Rapidly eliminated volatile anesthetics are undoubtedly the best choice Cyclopropane is one of the most suitable of the major agents Ethylene is preferred to nitrous oxide because of its greater potency, although the possibility of inducing anoxia exists with both drugs Ether may be used if necessary but is less desirable Local anesthesia, or various types of nerve blocks may be used if minimal amounts of local anesthetic drugs are used Spinal anesthesia may be used when jaundice of the obstructive type has been present for short periods of time When the jaundice is due to hepatitic disease or is accompanied by fever, weight loss, anemia, cachexia, dehydration, hypotension and so on it is best to avoid its use

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The renal epithelium is impermeable to serum proteins under normal circumstances After chloroform and ether anesthesia a transient albuminuria occurs in over half of the cases Casts and leukocytes may also be found occasionally Glucose rarely appears in the urine as a result of anesthesia

Histological changes in the kidney parenchyma ascribable to anesthetic drugs rarely occur save after chloroform anesthesia The possibility of lesions in the human kidney from the use of vinyl ether has been suggested but that it actually occurs has not been established

The response of the kidney to general anesthesia varies with the extent and depth of anesthesia The greater the depth, the more profound the change irrespective of the drug employed Recent work suggests that intrarenal vasoconstriction is largely responsible for the diminution in urinary output This is associated with a fall in glomerular filtration and a reduction in the excretion of electrolytes and water An increase in renal tubular reabsorption of both electrolytes and water occurs concomitantly Operation itself in the absence of shock and hemorrhage has little effect on renal function It is probable that whenever renal dysfunction occurs during the postoperative period it is due, not so much to anesthesia, as it is to other factors It is possible that anesthetics may affect the renal tubules so that in the postoperative period they are not able to properly manage reabsorption and excretion of electrolytes and fluids Spinal anesthesia does not have any appreciable effects upon renal function

## EFFECT ON DISEASED KIDNEY

Little data are available on the effects of anesthetics upon the diseased kidney Consequently there is little information which can be used as a guide for the selection of anesthesia in patients with renal disease and dysfunction In considering the choice of anesthesia for patients with kidney disease the selection must be based upon the physiologic disturbances present as a result of the disease, namely cardiovascular disturbances, particularly alterations in blood pressure, edema, ascites, anemia, and changes in electrolyte concentration

## NEPHROSIS

Nephrosis may complicate surgical diseases or vice versa When nephrosis is present, edema, lowered metabolic rate, severe anemia, lowered serum proteins, and often ascites are the chief findings Occasionally pneumococcus peritonitis and alterations in blood pressure are present Anesthetic techniques which disturb acid base balance should be avoided Anoxia and carbon dioxide retention are to be avoided Anesthetics which alter blood

pressure, particularly those which cause it to fall, are not desirable Spinal anesthesia is not a wise choice if the disease is severe or has been long standing particularly *if ascites is present* Increased intra abdominal pressure is a contraindication to spinal anesthesia In addition anemia is also a contraindication to spinal anesthesia Severe *hypotension which may be* followed by irreversible circulatory collapse is a strong *possibility*

The best choice of anesthesia in cases of lipoid nephrosis is cyclopropane Rapid induction and recovery follows with little or no disturbances in blood chemical constitutents Ethylene with adequate concentrations of oxygen combined with ether may be used but *is followed by slow recovery* Minor procedures may be performed using local anesthesia Non volatile drugs are best avoided because of the prolonged depression which may occur Disturbances in function are prolonged by slowly eliminated drugs The inability of a diseased kidney to excrete drugs which are eliminated unchanged into the urine *must be borne in mind* Even in the case *of drugs which are* destroyed by the liver it has been noted that when renal disease is present something happens and there is prolonged depression irrespective of the fact that the kidney is supposed to have no part in its elimination

## CHRONIC GLOMERULONEPHRITIS

Acute nephritis most frequently complicates streptococcal infections which may on occasion require surgical intervention Anuria, oliguria, hematuria, edema, elevation in blood pressure, fever, signs of sepsis, anemia, and azotemia may be present and are factors to be considered from the stand point of anesthesia In seriously, acutely, ill subjects local *infiltration is the* best choice if the operation can be performed with it Where local anesthesia cannot be used cyclopropane is the drug of choice It is labile and permits rapid induction and recovery and causes little or no metabolic disturbances Any suppression in urinary function is quickly restored to normal due to the rapid recovery Ether is less desirable because its effect *on the urinary* output may be sustained over a longer period of time due to slow recovery As a general rule *the use of spinal anesthesia* is not advised particularly [illegible] an elevation in blood pressure, anemia, sepsis or uremia are present Occasionally spinal anesthesia promptly ameliorates renal vascular [illegible] in acute nephritis with hypertension Non volatile drugs *such as* [illegible] paraldehyde and long acting barbiturates are contraindicated Ul[illegible] acting barbiturates may cause prolonged *somnolence* and a prolonged [illegible] of suppression of renal function and are, therefore, best avoided.

## NEPHROSCLEROSIS

Malignant nephrosclerosis with severe hypertension [illegible] plicates surgical diseases The elevated blood *pressure,* [illegible] ment, anemia, and cardiac disturbances are of *concern* [illegible]

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are accompanied by fever and other signs of sepsis more often than not When the disease is unilateral and renal *insufficiency is absent the choice* of anesthetic differs little from that for other septic conditions Cyclopropane, thiopental combined with nitrous oxide, or ethylene with or without ether, spinal or nerve blocks may be used When accompanied by anemia, hypertension or signs of renal insufficiency, the choice is the same as for acute and chronic nephritis

## TUBERCULOSIS OF THE KIDNEY

Anesthesia for surgical patients who have this complication, even if not complicated by pulmonary tuberculosis, is *managed in the same manner* as pulmonary tuberculosis, largely on the assumption *that it may be associ*ated with it although clinical and laboratory findings do not suggest it When the disease is far advanced and renal insufficiency is present the choice of anesthesia differs little from that outlined for nephritis Anemia, fever, weight loss and renal insufficiency are complicating factors which must receive due consideration Cyclopropane, ether or spinal anesthesia may be used Thiopental with nitrous oxide may also be used

## NEOPLASMS OF THE KIDNEY

Inasmuch as renal neoplasms do not disturb kidney function unless they are bilateral, which, of course is unusual, and they inactivate or destroy the major portion of the existing renal tissue, selection of anesthesia presents no particular problems when they are present Usually neoplasms are unilateral and the uninvolved kidney is functioning normally The selection is then governed by the nature of the requirements for this operation (The choice of anesthesia for nephrectomy is outlined in Part III ) When the disease is extensive and anemia and emaciation are present the choice must be made according to these factors and the status of the patient

## DEGENERATIVE LESIONS OF THE KIDNEY

Structural changes of the kidney such as cloudy swelling, tubular degenerations due to mercury and other poisons, fatty and amyloid degeneration give rise to various symptoms which arise from the dysfunction they cause Anesthesia under such circumstances is managed on the basis of the resulting disturbance in function In the absence of anemia, elevation in blood pressure, nitrogen retention, loss of concentrating power and so on, the choice of anesthesia differs in no way from that outlined for un*complicated surgical* diseases Should any of these complications be present anesthesia is then managed according to the recommendations previously outlined for renal dysfunction and its complications

Anesthetics which elevate blood pressure or which disturb acid base balance are to be avoided Nitrous oxide and ethylene are not easily administered without anoxia Anoxia and carbon dioxide retention are to be avoided The use of spinal anesthesia is not advised because it may cause a precipitous fall in blood pressure The question in these cases is what will do the patient the least harm rather than what is best.

## UREMIA

Renal insufficiency is encountered in surgical patients preoperatively from time to time Although it may be due to extrarenal factors, more often it is associated with the lower nephron syndrome or long standing renal disease Early renal shut down usually presents no serious problem as far as anesthesia is concerned but long standing insufficiency with well estab lished uremia does Coma, convulsions and acidosis are the three most im portant factors in uremia as far as anesthesia is concerned Stomatitis and ulceration of the mouth are also worthy of note from the standpoint of laryn goscopy and use of airways Drugs such as thiopental should be avoided because they cause respiratory depression and prolonged somnolence Cyclopro pane or ethylene with oxygen are the least harmful of the gases Neither en hances acidosis Local or regional anesthesia, if they can be used and permit the surgeon to work without handicap, are desirable choices Any drug or tech nique which enhances acidosis is to be scrupulously avoided Chloroform, ethyl chloride or trichlorethylene should not be used Techniques which do not permit adequate oxygenation and control of carbon dioxide tension are not to be used The muscle relaxants are contraindicated

## SENILE NEPHROSCLEROSIS

Senile nephrosclerosis is probably unrecognized and frequently en countered particularly in old patients It is accompanied by little or no hypertension or renal insufficiency Under such circumstances the choice of anesthesia presents no particular problem It is unusual for it to exist alone, however Other manifestations of degenerative diseases particularly vascular lesions are present These influence the choice of anesthesia more than the renal disease In view of the fact that it is associated with arterio sclerosis, anesthetics which cause wide fluctuations in blood pressure, particularly spinal anesthesia are to be avoided Ether, cyclopropane thio pental with ethylene or nitrous oxide may be used Non volatile drugs and muscle relaxants may be used, if used cautiously

## SUPPURATIVE DISEASES OF THE KIDNEY

Suppurative diseases of the kidney parenchyma the pelvis and the ureter include infections such as pyelonephritis pyelitis or hydronephrosis These

# XXIII

# DISEASES OF THE CENTRAL NERVOUS SYSTEM

## BRAIN

### Psychoses

Diseases of the central nervous system characterized by psychotic manifestations occasionally complicate surgical problems Some organic lesions present symptoms which suggest functional disease and vice versa Functional mental disorders encountered are the psychoses, the neuroses and various psychopathic personalities The remarks in this discussion also apply to organic lesions of the brain which give rise to psychotic symptoms The psychotic patient who develops a surgical disease does not present any particular problem to the anesthetist unless he is disturbed to the point of being uncooperative Some patients appear to be cooperative and lead the physician into a sense of false security Their behavior may be acceptable until the moment of induction of anesthesia at which time they become unruly and violent General anesthesia is preferred in nearly all circumstances in dealing with psychotic patients It is advisable to use basal narcosis induced with an ultra short acting barbiturate intravenously or avertin rectally and maintain the hypnotic state until inhalation anesthesia is commenced The basal narcosis is induced at the bedside There is no particular preference concerning the choice or technique of supplementary anesthesia after basal narcosis has been induced That which suits the situation best is the one to use The use of regional anesthesia is not advised It is seldom satisfactory for any procedure of even those of the slightest magnitude in disturbed patients

### Drug Addiction

#### Alcohol Addict

The chronic alcohol addict is difficult to anesthetize with aliphatic anesthetics Such addicts appear to be resistant to hydrocarbons, ethers, alcohols, halogenated aldehydes and halogenated alcohols Presumably a cross tolerance develops between alcohol and other drugs of the aliphatic type Inhalation anesthesia in alcohol addicts is characterized by a prolonged second stage and an extremely narrow zone of third stage Sometimes the zone of the third stage is so narrow that the patient appears to pass from stage II to stage IV without ever having been in stage III It is advisable to avoid inhalation anesthesia and basal narcosis with the aliphatic drugs when anesthetizing chronic alcohol addicts Spinal and regional anesthesia should

## REFERENCES

ADRIANI JOHN *Chemistry of Anesthesia* Springfield Thomas, 1950, p 392

CRAWFORD E J GAUDINO M Changes in extra fluid volume, renal function and electrolyte excretion induced by intravenous saline solution in short periods of anesthesia *Anesthesiology 13* 374–388 1952

PAPPER E M Renal function during general anesthesia and operation *J A M.A*, *152* 1686 1953

SMITH, H W ROVENSTINE E A GOLDRING W *et al* The effects of spinal anesthesia on the circulation in normal unoperated man with reference to autonomy of the arterioles and especially those of the renal circulation *J Clin Investigation 18* 319 1939

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be used whenever possible Chronic alcohol addicts do not necessarily manifest tolerance to all central nervous system depressants They may respond in the expected manner without increased tolerance to therapeutic doses of narcotics and barbiturates Overdosage may easily result when thiopental is used for basal narcosis in these subjects if one assumes that larger than average doses are required because of the addiction

When inhalation anesthesia cannot be avoided in dealing with chronic alcohol addicts basal narcosis with alcohol or thiopental simplify induction to a certain extent It is almost impossible to obtain satisfactory surgical anesthesia with nitrous oxide or ethylene in chronic alcohol addicts Cyclopropane alone is not always satisfactory for maintenance although it is the best for induction *A prolonged second stage invariably accompanies induction* of ether anesthesia Ethyl chloride, chloroform and vinyl ether are not satisfactory The muscle relaxants are useful adjuncts

The misconception that subjects with acute alcoholism are difficult to anesthetize is prevalent Surgical patients who have acute alcoholism are not difficult to anesthetize The alcohol acts as a basal narcotic and actually simplifies the induction of anesthesia

### Barbiturates

Habitues to barbiturates present no problem for the anesthetist When barbiturates are used for preanesthetic medication or basal narcosis for these patients larger than ordinary doses are required Inhalation anesthesia is tolerated by these subjects without any unusual manifestations Cross tolerance between barbiturates and aliphatic drugs is the exception rather than the rule

### Narcotics

Addiction to narcotics whether to the opium alkaloids, their derivatives or to synthetic substitutes presents no difficulty from the standpoint of anesthesia Premedication with narcotics is not advised if the addict is "cured" Basal narcosis with the thiobarbiturates or avertin is effective and may be used instead When narcotics are used for premedication for the addict who has not been under treatment the dose to which the addict is accustomed is the one to be used The prolonged eventful second stage characteristic of the alcohol addict is not observed when narcotic addicts are anesthetized with inhalation anesthesia

## Organic Diseases of the Brain

Organic diseases of the central nervous system merit special consideration from the standpoint of anesthesia Two factors must be considered, (1) the direct effect of the drug on the nervous elements and (2) the changes

in the hydrodynamics of spinal fluid In general any deleterious effect caused by the anesthetic upon the nervous system is due to an elevation in intracranial pressure Intracranial pressure is raised by (1) a rapid formation or an accumulation of excess cerebral spinal fluid, (2) increasing the volume of blood in the cerebrovascular system and (3) increasing fluid in the inter and intracellular spaces of the nervous tissues Any or a combination of these three factors raises the pressure in the cranial cavity Increases in pressure cause compression of the medulla against the base of the skull and a disturbance in function of vital centers This is followed by disturbances in circulation notably blood pressure, and respiration The two factors which cause an increase in intracranial pressure during anesthesia more than any other are *carbon dioxide excess* and *anoxia* The former exerts a more pronounced effect than the latter Most central nervous system depressants raise intracranial pressure, but the influence of the agent per se is negligible Most changes result secondarily from alteration of gaseous composition of the blood resulting from inadequate ventilation

## Cerebral Vascular Lesions

Vascular lesions of the brain occasionally complicate surgical diseases Hemorrhage whether spontaneous, or the result of trauma may be intracerebral, subarachnoid, subdural or extradural Irrespective of the etiology and type of lesion the one problem which is common to all of them from the standpoint of anesthesia is that of increased intracranial pressure Any anesthetic which increases intracranial pressure complicates matters Increased arterial blood pressure because of its secondary effects on intracranial pressure is to be avoided Whenever possible regional anesthesia should be used in such situations Spinal anesthesia is not suitable for two reasons (1) the circulatory changes precipitated by spinal anesthesia lead to hypotension and (2) lumbar puncture may be contraindicated When general anesthesia is necessary any technique which causes sub oxygenation or an increased carbon dioxide tension must be avoided An increased carbon dioxide tension is difficult to avoid when drugs which cause hypoventilation such as cyclopropane or thiopental or the narcotics are used unless mechanical tidal air regulation is available Respiratory acidosis invariably accompanies hypoventilation Difficult prolonged induction with ether may cause an elevation of intracranial pressure Ethylene or nitrous oxide are innocuous when administered without anoxia However one is never certain that this objective may be accomplished, unless basal narcosis is used and this may cause hypoventilation Premedication with the narcotics may raise intracranial pressure secondarily to hypoventilation The question resolves itself into which drug or technique will do the least harm rather than which is the best The proper selection is often difficult to make

### Thrombosis

The anesthetic management of patients with thrombosis of the cerebral vessels differs in no way from that due to hemorrhage Emboli cause venous or arterial obstruction which may be followed by increased intracranial pressure Anesthetics or techniques of administration which raise intra cranial pressure are to be avoided Rapid uneventful induction with ethylene or cyclopropane which has been preceded by basal narcosis with avertin or thiopental is the procedure to be used when general anesthesia is desired

### Intracranial Aneurysms

The presence of unruptured intracranial aneurysms whether congenital, mycotic or atheromatous presents a serious situation from the standpoint of anesthesia Drugs or manipulations which disturb the dynamics of cerebral spinal fluid pressure, blood pressure or blood flow in the cranial vault may lead to rupture Elevation of blood pressure from struggling, excite ment, carbon dioxide, excess anoxia or vasopressor drugs should be avoided Induction of general anesthesia should be preceded by basal narcosis with thiopental or avertin to avoid excitement It is advisable, as a rule, to omit narcotics for premedication because they may cause a respiratory depres sion which leads to anoxia and carbon dioxide retention both of which causes an increase in cranial pressure Hypotensive agents may be used pre oper atively and as adjuncts to anesthesia

## Hydrocephalus, Cerebral Edema etc

Patients who have hydrocephalus, cerebral edema due to systemic disease, lacerations and other trauma to the brain, edema due to toxic reactions from drugs and other noxious agents or anoxia usually present a picture and clinical manifestations which can be ascribed to increased intracranial pres sure Factors which further increase the intracranial pressure should be avoided The management of patients with these conditions is identical to the management of anesthesia in patients who have vascular lesions

## Neoplasms of the Brain

Tumors of the brain and other expanding intracranial lesions present the same problems in the management of anesthesia which arise when vascular disturbances are present The intracranial pressure may be elevated and further increased by inexpert management Manipulations and drugs which further increase intracranial pressure are to be avoided These patients are often comatose, have palsies, convulsions and other neurologic signs Psychotic manifestations may be present Local anesthesia is the most desirable choice for comatose patients If local anesthesia is not practical basal narcosis using tribromethanol or thiopental supplemented with nitrous oxide and ether may be used Hypoventilation is to be avoided Cyclopro

pane may be used with assisted respiration *If asymptomatic the same pre cautions should be exercised* The management of anesthesia for intracranial operations is described in Chapter XXIX

## Suppurative Diseases of the Brain

Suppurative processes within the cranial vault such as brain abscess, suppuration in the venous sinuses, sinus thrombosis, meningitis due to pyogenic bacteria or tuberculosis present identical problems to those arising from vascular lesions—those due to increased intracranial pressure In addition there are symptoms of sepsis, mental disturbances, spasticity, rigidity and other neurological signs which, of course, complicate the man agement of anesthesia Management however is the same as with vascular lesions Anesthetics which increase the intracranial pressure least are to be used Whenever possible local anesthesia is the desirable choice

## Inflammations of the Brain

Encephalitis complicating surgical diseases is uncommon Fever, sepsis, coma, respiratory, circulatory and neurologic disturbances may be present Aggravation of these may be avoided by minimizing increases in intracranial pressure Excitement, struggling, anoxia and carbon dioxide excess are to be avoided For this reason when general anesthesia is desired basal narcosis with thiopental or avertin may be used if the patient is not comatose and has no derangements of respiratory pattern of central origin This may be followed by cyclopropane Ether may be used for maintenance An intra tracheal airway should be available in the event respiratory failure ensues Whenever possible, local infiltration or nerve block should be used Data concerning the use of spinal anesthesia in patients who have diseases of the central nervous system are meagre As a general policy spinal anesthesia is avoided under circumstances such as these

## Diseases of the Basal Ganglia

Diseases of the basal ganglia such as Parkinsonism, chorea, Wilson's dis ease, pseudosclerosis, and so on which are manifested by neuromuscular disturbances merit special consideration Belladonna alkaloids or other drugs which minimize neuromuscular responses are administered preopera tively Such patients may then be anesthetized with any desired drug, usually one which is rapid acting The ultra short acting barbiturates are avoided because they may enhance the tremors Cyclopropane, ethylene, nitrous oxide or avertin may be used Spinal anesthesia may be difficult to induce Besides, its use in diseases of the central nervous system is unwise

## Epilepsy

Patients with epilepsy and related disturbances of the motor cortex are best managed by using general anesthesia Preanesthetic sedation with a

barbiturate such as phenobarbital or other anti convulsant drug is advised The patient is then anesthetized with as little excitement as possible Basal narcosis with avertin or thiopental may be necessary to make the induction of anesthesia simple and rapid Cyclopropane alone or ethylene followed by ether may be used There is no contraindication to the use of muscle relaxants Local infiltration or nerve block may be used if basal narcosis using barbiturates intravenously is used in conjunction with the block Vinyl ether, and carbon dioxide excess are to be avoided because they may initiate convulsions

## CEREBELLUM

Anesthesia for patients who have lesions in the cerebellum whether of vascular origin, or due to trauma, suppuration or inflammation, are managed in the same manner as similar conditions in the cerebrum

## INFLAMMATORY AND DEGENERATIVE LESIONS OF THE CORD

Diseases of the spinal cord are of special concern to the anesthetist Spinal anesthesia is scrupulously avoided even though there is no evidence that local anesthetic drugs enhance existing diseases of the spinal cord Irrespective of the nature of the lesion or disease whether it be due to syphilis, myelitis, disseminated sclerosis, combined degeneration, syringomyelia or neoplasm, lumbar puncture and intrathecal injections are avoided Instances of damage to the spinal cord or paralysis after spinal anesthesia have been associated with pre existing neurologic disease It is possible for a patient who is not aware of an existing subclinical neurologic disease to become conscious of symptoms after surgery and ascribe them to the spinal anesthetic From a medicolegal point of view, if for no other reason, spinal anesthesia is to be avoided when known neurologic lesions are present

### REFERENCES

AYRE P Anesthesia for intracranial operations *Lancet* *1* 561 1937

HOLLAND W S PAPPER E M Circulatory changes during anesthesia for neuro urgical operations *Anesthesiology* *13* 343–352 1952

# XXIV

# DISEASES OF THE SKELETAL SYSTEM

## MUSCLES

Diseases of muscles of interest to anesthesiologists fall into two categories, those characterized by hypertonus, rigidity or spasm and those characterized by hypotonia, asthenia or atony Diseases characterized by hypertonus and spasticity offer no particular problem from the standpoint of anesthesia except that during induction spasm of the laryngeal and pharyngeal muscles may interfere with proper maintenance of the airway Drugs which permit rapid induction such as cyclopropane or thiopental combined with a muscle relaxant are to be used Nitrous oxide or ethylene used alone are not, as a rule, satisfactory Regional anesthesia is suitable for minor procedures but, in general, unsatisfactory Barbiturates or avertin may be used for basal narcosis Spinal anesthesia may be used provided one is certain of the diagnosis and cord lesions have been excluded Carbon dioxide excess tends to increase muscle tone and must be avoided

Patients with diseases characterized by atonia or flaccidity may develop hypoventilation or respiratory paralysis when anesthetized Controlled respiration may be necessary during and possibly after operation Prolonged controlled respiration may lead to circulatory failure if ventilation is not adequate This must be borne in mind when long operations are contemplated Drugs which act rapidly, are labile and are eliminated quickly, are preferred to slow acting, slowly eliminated drugs Ether is objectionable from this standpoint The gases are undoubtedly the best for these patients Cyclopropane is ideal The non volatile drugs are objectionable because they are uncontrollable, may cause hypoventilation and prolonged depression The use of muscle relaxants is not advised

*Myaesthenia gravis* complicates surgical diseases more often than is realized Cessation of respiratory efforts occurs promptly after induction regardless of the anesthetic drug used These patients are non resistant to central nervous system depressants

Any drug may be used for these patients although cyclopropane is the drug of choice for major surgery For minor surgery local infiltration, nerve blocks ethylene or nitrous oxide may be used When general anesthesia is used a drug which is rapidly eliminated is one that should be chosen so that recovery may be as prompt as possible Preliminary medication with a combination of atropine and prostigmine are advised The same medication should be used after the operation is over The muscle relaxants are strictly contraindicated in patients who have myaesthenia gravis because

they induce an intense, sustained effect There is no objection to the use of low spinal anesthesia

## BONES AND JOINTS

The two most commonly encountered diseases of the joints are osteo arthritis and rheumatoid arthritis The infectious arthritides, degenerative changes of joints, particularly when limited to single joints or joints of the extremities offer few problems as far as anesthesia is concerned Osteoarthritis of the spine complicates spinal anesthesia and renders attempts at lumbar puncture difficult Outside of that, this condition offers very little trouble from the standpoint of anesthesia

Rheumatoid arthritis may cause difficulty in positioning due to limitation of motion, particularly if the knees, hips or spine are involved In addition lumbar puncture may be difficult or impossible When the cervical spine is involved the head cannot be extended Attempts at intubation and main taining a patent airway are often impossible When so, tracheotomy may be indicated Associated systemic manifestations characteristic of the acute phase of, or the exacerbations of rheumatoid arthritis such as anemia, fever, enlarged spleen must be considered, if present, in selection of anesthesia When the disease has run its course the ankylosis of the joints and the limitation of motion are the chief concern of the anesthetist No special drug or technique is indicated or contraindicated

Diseases of the bone or cartilage or systemic diseases causing skeletal de formities such as acromegaly, dwarfism, giantism, Paget's disease, or exos tosis may cause difficulty in placing the mask on the face, may render lumbar puncture difficult or may cause obstruction of the airway Otherwise there are no particular problems as far as anesthesia is concerned

### REFERENCES

Primer on rheumatic diseases *J A M A* *152* 323 1953

Kurtecs J G Whitehouse S Cerzosimo F Anesthesia for the paraplegic patient *J A M A* *141* 639–642 1949

# XXV

# DISTURBANCES OF THE ENDOCRINE SYSTEM

The endocrine glands are so inter related that disturbances in function in one glandular structure are often reflected by hypo or hyperfunction in others The most important glands and the ones about which the least information is available from the standpoint of anesthesia are the adrenal and the pituitary

## THE ADRENAL

When adrenal insufficiency exists the possibility of sudden circulatory collapse and death is ever present although fairly adequate substitution therapy is now available Well established Addison s disease is not commonly encountered as a complication of surgical diseases, fortunately, but when it is, it presents a serious problem from the standpoint of anesthetic management More dangerous than a well recognized case of Addison's disease is the insidious latent unrecognized case of adrenal insufficiency Deaths occurring without any apparent cause have been explained by assuming the presence of this entity Minimum premedication should be used for patients known to have adrenal hypofunction It has been shown that adrenalectomized animals manifest a greater sensitivity to hypnotic and anesthetic drugs than those with intact adrenal glands Laboratory data indicate that severe, often irreversible, circulatory collapse ensues quickly during ether anesthesia in adrenalectomized dogs Adequate preoperative preparation with adrenal hormones and saline and dextrose is indicated before surgery

Anoxia carbon dioxide excess manipulations leading to fear, fright, blood loss or trauma are to be avoided Procedures or drugs which cause the blood pressure to fall, such as spinal anesthesia avertin and the barbiturates are to be avoided The method and technique of administration is probably more important than the choice of drug although rapidly eliminated drugs are preferred Cyclopropane is probably the best choice because it is rapidly eliminated is labile and anesthesia is rapidly induced Sufficient relaxation is obtained with ease because these patients are asthenic and non resistant Sudden circulatory collapse must be anticipated at any moment from the beginning to the end of the procedure Hormones and vasopressors must be immediately available for treatment of circulatory collapse Although data on the subject are meager muscle relaxants should be used with caution if at all

Adrenal hyperactivity is occasionally encountered This is usually associated with chromaffinomas, the best known of which are the pheochromocytomas An excess of adrenal cortical hormones, epinephrine and epinephrine like substances are elaborated by the gland Paroxysmal elevations in blood pressure characterize the disease Hypoglycemic shock, also paroxysmal in character, may occur during which the excess hormones are liberated Anesthetics which cause the blood pressure to fall should not be used Anesthetics such as cyclopropane which increase cardiac irritability likewise are to be avoided The possibility of ventricular fibrillation is ever present Ether is the drug of choice for these cases Ganglionic blocking agents or sympatholytic agents should be available to reduce the blood pressure when it rises to excessively high levels

It is advisable to continue medication or to even increase the dose of cortisone and other adrenal cortical hormones which are being administered to patients for therapeutic purposes preoperatively The drug should be continued for several days postoperatively Adrenal insufficiency may develop if the medication is discontinued prior to the operation

## THE THYROID GLAND

Disturbances of the thyroid gland are characterized either by hyperactivity or hypoactivity Grave's disease with its increased metabolic rate and cardiac effects has been described in Part III under thyroidectomy Anything which causes sympathetic overactivity of any sort must be avoided when thyrotoxicosis is present The high metabolic rate and increased oxygen consumption must be considered in selecting and managing anesthesia Anesthetics which increase cardiac irritability, or sympathetic activity are undesirable Epinephrine and related amines must not be added to solutions of local anesthetics used for nerve blocking and infiltration The patient should be well sedated in order to minimize apprehension and psychic disturbances which give rise to extreme degrees of tachycardia and, on occasions, arrhythmias

Hypoactivity of the thyroid gland results in myxedema The low metabolic rate, the thick tongue, the increased lymphoid tissue, thickened mucous membranes, myxedema of the skin, the cardiac changes and related glandular disturbances are to be taken into consideration when selecting anesthesia for patients with well defined hypothyroidism Except in the case of dire emergencies, surgery should be deferred for several days and therapy instituted with thyroid extract Obstruction of the airway occurs from the edema, lymphoid tissues, and thick membranes in the oro and hypopharynx

These patients are usually much less tolerant to depressant drugs than normal Comparatively speaking, less than the average quantities are required to cause them to be relaxed Blood pressure may be low and further decreases may be encountered due to drug action At times it may be diffi

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cult to maintain the blood pressure at normal levels Spinal anesthesia, and anesthetic and hypnotic drugs which lower the blood pressure should not be used Premedication should be used cautiously Usually half the normal dose is used Where the hypothyroidism is mild selection of anesthesia offers no serious problem Patients manifest little deviation from the normal except that smaller quantities of drugs are required

## THE PARATHYROID GLANDS

Disturbances of the parathyroid glands, as in the case of other endocrine glands, are characterized by hyperactivity or hypoactivity Hyperactivity of the parathyroid glands results in increased blood calcium, renal insufficiency and the development of bone cysts There may be a hypoactivity of the nervous system Convulsions are not present In general there are no particular problems of concern to the anesthetist The drug and technique to be selected is the one which is suitable for the circumstances

In hypoactivity of the parathyroid gland blood calcium is reduced Tetany and other manifestations of increased irritability of the central nervous system may be present These patients should be given ample sedation with barbiturates and narcotics preoperatively and prepared with dihydrotachysterol Calcium should be given preoperatively and during anesthesia to reduce the irritability In emergencies, parathormone can be given Precautions to avoid hyperventilation should be instituted to minimize alkalemia There is no particular choice or contraindication of anesthetic drugs in these patients, however The one which meets the needs of the moment may be used

## THE PITUITARY GLAND

The pituitary gland may also show manifestations of hyperactivity or hypoactivity When the gland is hyperactive disturbances in growth and metabolism, particularly diabetes, are the most prominent manifestations Gigantism is common in certain pituitary tumors Gigantism is of little concern from the standpoint of anesthesia It offers no problems except that large masks, airways and laryngoscopes may be needed When hyperactivity comes on late in life acromegaly develops instead of gigantism The distorted bones, exostoses, hyperplasia of the connective tissue, enlarged lips, tongue, hands and feet may present problems from the standpoint of maintaining a proper airway and intubation during general anesthesia In performing nerve blocks the landmarks are frequently distorted making the procedure less precise As far as general anesthesia is concerned, there is no particular choice or objection to any of the currently used anesthetic drugs

When hypoactivity of the pituitary gland is present metabolism is reduced and obesity may be present The problems of anesthesia are of those

of obesity and low metabolic rate described under hypothyroidism The patients are not resistant to drugs and less than usual is required Dysfunction of the pituitary may result in changes in activity of the adrenal gland Consequently this possibility must be explored in these patients and anesthesia managed accordingly

## THE THYMUS

The function of this gland is not known Unlike the other glands hyper- or hypofunction, if either exists, bears no known relationship to anesthesia An enlarged thymus presents no particular problem to the anesthetist except that it may compress the trachea and obstruct the airway, particularly if the mass is large Status lymphaticus has been ascribed as a cause of sudden death during anesthesia The general feeling is that this syndrome, if it exists, and many physicians feel that it does not, bears no relationship whatever to sudden and unexpected death

Myaesthenia gravis may be associated with an enlarged thymus gland Thymectomies have been performed in an attempt to cure the disease These operations have been uneventful The contention that sudden death and thymic enlargement are inter-related is not borne out by the experiences with thymectomy Thymectomies present no special problem to the anesthetist Cyclopropane or ether intratracheally may be used when the thymus is enlarged and the patient is being operated upon for thymectomy for myaesthenia gravis Basal narcotics may be used Muscle relaxants obviously are contraindicated Local anesthesia cannot be used because the operation is too extensive and of great magnitude

## THE SPLEEN

Splenomegaly is associated with other systemic diseases particularly blood dyscrasias and the management of such patients is in accordance to those outlined for the associated diseases Splenomegaly presents no problem as a rule to the anesthetist except in certain blood dyscrasias These problems have been described in Chapter XXIII

### REFERENCES

DUNDEE J W Thiopental in Addison s disease *Brit J Anaesth*, *23* 3 1951
KLEITSCHE W P Evaluation of toxic thyroid patient *Postgrad Med*, *9* 394 1951
LUNDY J S Cortisone problems involving anesthesia *Anesthesiology* *14* 376–380 1953
NASH J *Surgical Physiology* 2nd Ed Springfield Thomas 1953
PAPPER E M, CAHILL G Anesthetic Problems in Hormonal Disturbances of the Adrenal Glands *J A M A*, *148* 3 1952

# XXVI

# ALLERGY

Allergies are common in surgical patients and occasionally complicate the management of anesthesia Bronchial asthma, hay fever, angioneurotic edema, urticaria and other cutaneous lesions are the most common manifestations of the allergic state encountered

As far as is known, well defined instances of allergy to volatile anesthetics are very rare indeed Allergy to non volatile drugs is uncommon also Untoward responses to drugs usually ascribed to allergy are really due to overdosage or intolerance Allergy is more common with local anesthetics than general The manifestations however are cutaneous rather than systemic Syncope, convulsions and circulatory collapse from local anesthetics are due to overdosage or intolerance Cutaneous lesions are usually manifestations of repeated rather than single exposures to local anesthetic drugs This is more common in physicians and dentists than in patients

As a rule hay fever presents no serious problems from the standpoint of anesthesia The engorged mucous membranes of the nose and pharynx, the secretions, particularly the postnasal drip, may interfere with maintenance of the airway or cause laryngeal spasm when spasmogenic drugs such as thiopental are used Surgery should be deferred until the condition is relieved or subsides Likewise surgery should be deferred when the patient has an attack of bronchial spasm

Patients who have a history of being allergic but who show no manifestations of allergy at the time of operation present no problem to the anesthetist Patients who have hay fever should be premedicated with an antihistaminic drug and a belladonna alkaloid besides the narcotic The choice of anesthetic drugs and method of administration is immaterial The management of patients who have bronchial asthma has been described under the section on pulmonary diseases (Chap XIX) Spasmogenic agents such as cyclopropane or thiopental are to be avoided because they tend to induce or aggravate any existing bronchial spasm Meperidine is preferred to morphine because it is spasmolytic Operations on patients who have angioneurotic edema should be deferred until the condition subsides

## REFERENCES


BRENNEMAN R E Anesthesia for allergic patient *Ann Allergy, 7* 534 1949

CARON H C Anaphylaxis in anesthesia *Anesthesiology 8* 625–635 1947

STEIN, H B Ether allergy *Anesthesiology, 6* 515–520 1945

# XXVII

# INFECTIOUS DISEASES

## INFECTIOUS HEPATITIS

Infectious hepatitis is encountered in surgical patients from time to time particularly in cases where an error in diagnosis has been made and laparotomy is performed in the supposition that the patient has obstructive jaundice The anesthetic management of such patients is as described in the discussion on jaundice (Chap XXI) Patients who have homologous *serum jaundice are managed in the same manner as those with hepatitis,* jaundice and hepatic insufficiency from other causes

## TYPHOID FEVER

Typhoid fever occasionally complicates a surgical disease of emergency nature which requires immediate operation These patients may be acutely ill, have fever, are dehydrated, and have weight loss They are often referred to as "toxic" Toxic myocarditis due to the infection may be a complicating factor The management of anesthesia in patients with typhoid fever offers no difficulty Usually such patients are non resistant and require less anesthetic than normal individuals Infiltration or nerve block is used whenever possible Cyclopropane is more desirable than ether though the combination of the two is satisfactory It is best to avoid the non volatile drugs because of the possibility of prolonged depression in the post operative period Spinal anesthesia may be used in the convalescent or mildly ill patient but not in the acutely ill subject

## TETANUS

Patients with tetanus frequently require surgery for debridement, gastrostomy, tracheotomy and other procedures Mild forms of the disease may present no problem The anesthetic management of patients with well established tetanus may be difficult External stimulation of any sort may initiate severe convulsions and generalized rigidity of the muscles and intense spasm Obstruction to respiration results from pharyngeal and laryngeal spasm Spasticity of the jaws does not permit the reestablishment of the airway and asphyxia is likely to occur The marked muscular activity places considerable burden on the cardiovascular system

A rapid induction with cyclopropane or thiopental is desirable Muscle relaxants may be necessary to overcome rigidity Instrumentation with airways, laryngoscopes and endotracheal tubes must be avoided particularly when anesthesia is light Nerve blocks and local infiltration are not satisfac

tory unless basal narcosis is used as an adjunct Spinal anesthesia is not only difficult to induce but not advised whenever the central nervous system is involved in any way Vinyl ether may be used Ethyl ether may be used if preceded by a rapid acting induction agent such as ethylene, cyclopropane or vinyl ether Laryngeal spasm may occur if thiopental is used as an induction agent for ether

## PERTUSSIS

Adult surgical patients with pertussis are uncommon Occasionally children with whooping cough may develop a surgical disease requiring emergency surgery Wherever possible local anesthesia should be used when this complication is present Any stimulus in the upper respiratory tract whether it be an irritating gas, or vapor, secretions or mechanical instrumentation may initiate a paroxysm of cough and intense bronchial spasm Non irritating inhalation anesthetics such as cyclopropane, ethylene or nitrous oxide are to be used in preference to the volatile liquids which are more reflexogenic and stimulate mucous formation The thiobarbiturates are best avoided because they, too, are spasmogenic

## SCARLET FEVER

Scarlet fever is rarely encountered in surgical practice Patients with scarlet fever may require anesthesia for complications resulting from the streptococcal infection They usually present no anesthetic problem unless very "toxic" Sepsis and suppurative lesions in the ears or respiratory tract are the usual complications which may require surgery For minor procedures infiltration or nerve block may be used When general anesthesia is desired cyclopropane, nitrous oxide ether or ethylene ether or basal narcosis of thiopental with nitrous oxide may be used The anesthetic management of these patients presents no problem other than those peculiar to patients with sepsis from other causes

## DIPHTHERIA

Patients with diphtheria, may manifest signs of respiratory obstruction from the membrane characteristic of the disease which forms in the upper respiratory tract Also to be considered by the anesthetist is the possibility of toxic myocarditis On occasions the toxin causes palsies of cranial and spinal nerves, particularly the vagus Obstruction due to partial paralysis of the vocal cords or paralysis of the soft palate and fauces may occur Regional anesthesia is the most desirable choice for these patients When regional anesthesia cannot be used and general anesthesia is required cyclopropane may be used If there is considerable deposit of membrane and obstruction is present endotracheal catheterization may be necessary In the event diphtheritic myocarditis exists local or nerve block supplemented with

ethylene or nitrous oxide with some basal is satisfactory The use of cyclopropane is not advised because of its effect on the heart Ether is satisfactory from the standpoint of cardiac effects but a non traumatic induction is not always assured Thiopental and other drugs depress respiration The barbiturates are spasmogenic The presence of the membrane may initiate spasm

## MUMPS

Mumps may occasionally be complicated by a surgical disease requiring urgent operation The enlarged glands cause technical difficulties because the mask is difficult to apply and obstruction of the airway may easily occur Regional anesthesia is the most desirable choice and should be used whenever possible Cyclopropane or the nitrous oxide thiopental combination are the most desirable choices when general anesthesia is required

## VINCENT'S ANGINA

Vincent's angina complicates anesthesia by the presence of the lesions in the mouth If inhalation anesthesia is used airways, laryngoscopes and endotracheal catheters may inflict trauma and cause bleeding and possibility of dissemination of infection Whenever possible regional anesthesia should be used

## SYPHILIS

Syphilis presents no problem in the latent phases When lesions exist on the face or at the site of puncture the management is as outlined under diseases of the skin When tertiary lues is present and the cardiovascular system is involved the anesthetic management is as outlined under cardiac diseases Spinal anesthesia should not be used when the central nervous system is involved

## EXANTHEMA

Patients with measles offer no particular problem in regards to anesthesia in the convalescent period In the early stages, inasmuch as the manifestations are largely those of acute upper respiratory tract infection, the management and selection of anesthesia is as outlined in the section on acute respiratory infections (Chap XIX) Anesthetics which tend to cause laryngeal spasm such as the thiobarbiturates and cyclopropane are best avoided Non-irritating non spasmogenic drugs, such as nitrous oxide or ethylene are preferred

The other exanthemata such as variola, varicella, rubella and so on offer no particular problem as far as choice of agent is concerned unless the lesions about the face are severe or extend into the mouth

In this case application of masks and use of airways may present difficulties Regional anesthesia is used if possible otherwise intubation with the patient awake may be necessary after which general anesthesia may be

easily managed When the diseases are in the acute phase with fever, cyclopropane is the best choice Otherwise, nitrous oxide or ethylene ether or thiopental nitrous oxide may be used

## DISEASES OF THE SKIN

Diseases of the skin occasionally may present problems of concern to the anesthetist from at least two standpoints (1) Skin lesions may be manifestations of some systemic disease (2) Lesions may be present in areas which interfere with conduct of anesthesia in the usual manner When present, the possibility of allergy should be excluded The possibility that the drug and appliances used for anesthesia will not further aggravate the situation should be considered Non volatile drugs particularly may not be desired If the lesions are present at the site of a contemplated nerve block this form of anesthesia cannot be used If they are present over the back in the lumbar area spinal anesthesia cannot be used If present on the face the lesion may interfere with application of the mask When general anesthesia must be used in such situations intravenous anesthesia may be sufficient to perform a minor procedure Whenever intravenous anesthesia cannot be used, and inhalation anesthesia is indicated, an endotracheal catheter may be introduced while the patient is awake with the aide of topical anesthesia Anesthesia is then induced and conducted in usual manner If the lesions are on the face and head and are severe, a tracheotomy may be necessary and the inhalation anesthetic administered through the tracheotomy cannula

### REFERENCES

PULLEN, R. *Communicable Diseases* Philadelphia, Lea & Febiger 1950

## XXVIII

# THE EXTREMES OF AGE

The selection of anesthesia for patients at the extremes of age, presents problems which differ in many respects from those for the adult in the prime or at the peak of life During infancy the development of the organism is incomplete in many respects and certain important physiologic functions have not as yet established a normal pattern In senescence, many physiologic functions are in abeyance, and the reparative processes are at an ebb Selection and management of anesthesia must be modified to conform to these deviations

## *ANESTHESIA FOR GERIATRIC PATIENTS*

The number of surgical patients in the upper age groups has been increasing steadily during the past several decades This can, to a large extent, be ascribed to the increase in the life expectancy in the United States In addition, the attitude towards surgery for the aged has been modified considerably Surgical problems which formerly were only encountered on rare occasions, are seen daily in centers dealing largely with an aging population Besides, their management was not as well understood a few years ago as it is today Often these patients were considered inoperable and no attempt was made to perform surgery because the situations were termed desperate Better understanding of preoperative and postoperative care, improvements in surgical technique and refinements in anesthesia contribute largely to the successful results which are now obtained in situations heretofore doomed to failure The management of illness in the aged has become somewhat of a specialty in itself Whether or not this is necessary is questionable The medical and surgical problems encountered in patients in the older age group are actually every day medical problems One who is well versed in general medicine and familiar with pathologic anatomy and physiology is able to cope with the problems of disease in the aged

## DIFFERENCES BETWEEN THE AGED AND YOUNGER ADULTS

The choice of anesthesia for any patient young or old is made upon the basis of physical status Physical status is far more important than chronological age It is not unusual to have patients well advanced in years be in excellent physical condition and obviously good surgical risks On the other hand, middle aged patients are encountered who look much older than they actually are and present a variety of pathologic changes of a serious nature

The outlook for the successful outcome of a contemplated surgical procedure in these is obviously not as good as in the older patients. Attempts to prognosticate the outcome of a surgical procedure in the aged occasionally lead to embarrassment. A patient may appear to be one who will withstand a contemplated surgical procedure without difficulty. He may die unexpectedly postoperatively from a cerebral vascular accident, coronary thrombosis, a pulmonary embolus, shock, cardiac failure or other cause. On the other hand, a patient who appears to be an obviously poor risk, and one in whom a successful outcome or even survival is not anticipated frequently does surprisingly well. It is well to be cautious in any estimation of outcome or prognosis in a patient of advanced age, particularly.

## CLINICAL FACTORS INFLUENCING ANESTHESIA IN THE AGED

Some of the clinical factors which are peculiar to patients in the older age group which bear directly on the choice of anesthesia are (1) Cardiovascular status. Cardiovascular disease obviously is much more prevalent in old patients. The cardiovascular system does not respond to demands for increased work, changes in blood pressure, fluid loss and so on, as does the vascular system of the younger patient. As a rule the blood volume is reduced in the aged. (2) Problems of fluid balance are more difficult to manage in the aged than in younger adults. Overloading the vascular system with blood, plasma volume expanders and saline solutions may precipitate cardiac failure. (3) The respiratory system is deranged. Chronic pulmonary diseases may have been present for years in some cases causing ventilation to be inadequate. This is true particularly when chronic emphysema is present. The so called barrel chest interferes with adequate ventilation. Diaphragmatic movements are exaggerated and interfere with surgery in the upper abdomen. (4) Renal function has been reduced in many cases due to degenerative disease. Fluid, acid base and electrolyte balance may be disturbed. (5) Many old patients are not well nourished. Digestive disturbances may have caused weight loss and emaciation. Reduced serum proteins, vitamin deficiencies, or anemias may be present. (6) The functions of the liver may be disturbed. Patients in the older age group are unusually sensitive to certain of the central nervous system depressants particularly the non volatile drugs. This is presumed to be due to the inability of the liver to detoxify the drugs in a normal fashion. Consequently smaller doses of pre medication and basal narcotics are necessary in comparison to those needed for middle aged and young adults. (7) The metabolic rate declines gradually after the age of forty (Fig 31). It is well known that patients with reduced metabolic rate irrespective of age are more "sensitive" or less *tolerant* to central nervous system depressants than those with normal metabolism. (8) Changes, both structural and functional, may be present in

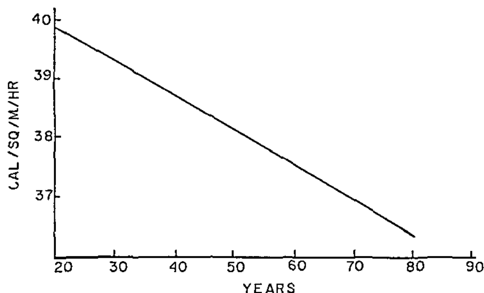



Fig 31 Curve showing the alterations in metabolic rate with increases in age Note that the metabolic rate declines gradually with advancing years after middle age

the central nervous system The cerebrum particularly shows changes due to vascular disturbances There may be psychic changes as a result Amnesic drugs and psychic influences of surgery may have adverse effects postoperatively (9) Deformities of the bones and joints and other alterations in skeletal structure may be present These may effect positioning attempts at lumbar puncture and intubation (10) Many patients in the upper age group are edentulous This causes difficulties in applying masks to the face when inhalation anesthesia is used A tight fitting closed system is difficult to secure Intubation may be necessary under such circumstances The edentulate patient is easy to intubate (11) The recuperative powers of the aged are as a rule diminished The convalescent period is longer Hypoventilation, since it leads to postoperative respiratory complications, is feared Early ambulation is often practiced in the aged to avoid postoperative circulatory and respiratory complications Anesthesia must be selected with this view in mind Analgesic drugs in quantities which do not cause respiratory depression in the postoperative period, must be used

## EFFECTS OF DIFFERENT ANESTHETICS IN THE AGED

In general, patients in the older age group are less tolerant to central nervous system depressants, both volatile and non volatile Ethylene, for instance, can rarely be used in a young and vigorous individual to secure relaxation without some degree of anoxia Relaxation, on the other hand, is secured more easily when the gas is administered to aged patients Satisfactory relaxation may be obtained for major surgery at times Both nitrous oxide and ethylene are suitable for patients in the older age groups provided the anesthetist administers adequate concentrations of oxygen with the gas Cyclopropane, in the absence of cardiovascular disease and hypertension,

is suitable for aged subjects because it is labile, allows adequate oxygenation and provides adequate relaxation The statement that cyclopropane cannot be used in the aged has no scientific basis Ether likewise is suited for the aged The only valid objection to the use of ether for aged subjects is that it is slowly eliminated Prolonged somnolence follows most operations except the briefest If early ambulation is desired, and it is in the aged, ether is a drawback Nausea, vomiting and general discomfort are more frequent after ether and cause the patient to be bedridden for a longer period of time postoperatively Ether predisposes to acidosis more than do the gases Vinyl ether may be used for short surgical procedures in the aged It is not recommended however for long major procedures requiring relaxation Chloroform and ethyl chloride are not recommended irrespective of the prevailing conditions Trichlorethylene may be used for analgesia but not for surgical anesthesia

Non volatile drugs such as avertin, paraldehyde and thiopental and most barbiturates are best avoided in the aged Prolonged depression is not uncommon when non volatile drugs are used for hypnosis or basal narcosis If used sparingly in as small a quantity as possible, they may cause no difficulties, but ordinarily they cause hypoventilation and hypotension Likewise the muscle relaxants are to be avoided or used with caution because they may induce hypotension and are eliminated slowly Succinyl choline is the best of the relaxants because of its evanescent effects due to rapid detoxification

Nerve block and infiltration anesthesia are suitable and the anesthetic of choice for many surgical procedures in the aged The use of a local anesthetic combined with epinephrine for surgery of the extremities is not safe practice The possibility of gangrene must not be forgotten particularly when peripheral vascular disease is present The use of spinal anesthesia depends largely upon the cardiovascular status of the patient As a rule low spinal anesthesia is tolerated reasonably well even when mild impairment of the cardiovascular system is present When an obvious, serious cardiovascular disease is present its use is not advised The aged do not withstand the circulatory derangements caused by high spinal anesthesia as well as younger subjects The compensatory mechanisms which operate to correct hypotensive states are not as effective as they are in younger subjects The aged do not compensate well and often manifest wide and extreme fluctuations in blood pressure The vasopressor drugs cannot be relied upon to correct the difficulties because they are not always as effective in the aged

## PEDIATRIC ANESTHESIA

There are a variety of reasons why pediatric anesthesia differs from anesthesia for adults Some of the chief reasons are these (1) The anatomy and physiology of the infant in many cases has not reached the full state

of development The effects of analgesic drugs are more variable and difficult to predict (2) Infants and children are usually more susceptible to the direct effects of surgery They do not tolerate blood loss, trauma, or reflex effects as well as the adult (3) Infants and children appear to be more susceptible to disturbances in ventilation Anoxia, asphyxia, carbon dioxide excess are not tolerated even in the slightest degree (4) The size of the subjects creates problems which are not easily solved Instruments used for pediatric anesthesia often must be modified to suit each individual Apparatus cannot be as easily standardized as that used for the adult An assortment of fittings, masks and endotracheal catheters must be available The apparatus must be designed to completely eliminate dead space in masks, fittings and catheters, otherwise rebreathing results Resistance in the apparatus must be minimal otherwise undue effort is necessary for respiration (5) There is greater possibility of psychic trauma in surgery of the child than that of the adult Preoperative medication, therefore, is important

The more remarkable differences between adults and children of concern to the anesthetist, then, are both anatomic and physiologic in nature Respiration in the premature infant is usually rapid and markedly irregular A periodic type of respiration similar to the Cheyne Stokes type is commonly observed This is believed to be due to various factors The respiratory center of the new born functions differently from the adult due to its incomplete development Differences exist in both the cross sectional area of the pulmonary capillary bed and alveolar structure present Total lung and functional residual air volume are less than in the adult Functional residual air volume is important The nearer it is to tidal volume the more rapid will be the mixing of gases The thoracic wall is soft and non-resilient Pressure or restraint of the mildest degree on the chest wall interferes with respiratory exchange

Differences exist in the responses of term and premature infants to carbon dioxide excess or a deficiency of or an excess of oxygen When pure oxygen is administered, the irregular breathing normally encountered is usually converted to the periodic type Respiratory rates and minute volume exchange of infants and children vary considerably They not only vary from child to child but in the same child from moment to moment A rate of 60 per minute is not uncommon Rates up to 120 are encountered at times in premature infants, particularly the smaller ones The tidal exchange may be as low as 10 cc per breath in many newborns The usual average tidal volume is between 12 and 18 cc per respiration

The blood volume at birth is approximately 10% of the body weight It thus differs little from that of the adult In the newborn this is subject to variation, however, depending upon the amount of blood which remains in the umbilical veins at the time the cord is severed The cardiac output is almost twice that of the adult in proportion to body weight The electrocardiographic pattern normally manifests an erratic ventricular preponder-

ance for the first several months of life Pulse rate in infants and children, likewise, is variable In the newborn the pulse rate often falls from 130 to 150 to about 100 a minute It is not uncommon to observe rates ranging up to 180 per minute At birth, blood pressure in the pulmonary artery is identical to that of the systemic pressure It changes gradually and at adolescence it approaches that of a normal adult, that is, approximately 1/6 of the systemic pressure The capillary network in the skin of infants and children is smaller than that of adults The resistance of the vessel wall is weaker in prematures than in full term babies and weaker in the new born compared to adults

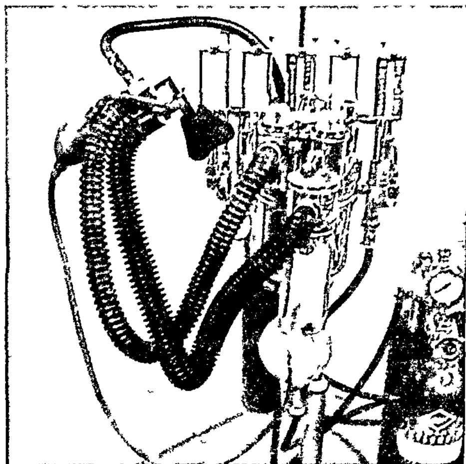
The hemoglobin of the fetus differs from that of the adult in chemical structure and behavior The difference in behavior is towards the affinity for oxygen At an inhaled oxygen tension of 40 millimeters of mercury the fetal blood oxygen is 75 per cent saturated Maternal blood at this tension is only approximately 50 per cent saturated The serum pH of plasma in the new born is lower than that of the adult This, of course, favors the unloading of oxygen from the red cell to the plasma The carbon dioxide tension in the fetus is slightly greater than that of the mother Fetal blood does not have carbonic anhydrase in the red cells

Renal function of the premature and the infant at term differs from that of the adult The new born infant does not elaborate the antidiuretic hormone in a normal fashion like the adult If water is withheld or given in excess new borns cannot concentrate and dilute urines as readily as adults Water loss occurs more readily through such a kidney because of the lack of concentrating power Renal function develops progressively after birth and maturity is probably reached in about 10 to 20 weeks

The metabolic rate of premature infants is slightly less in proportion to the body surface than that of infants at term The body temperature at birth approximates that of the mother After birth even though the infant is wrapped and placed in a warm environment the body temperature falls from 2° to 5°F after which it rises gradually to 98° or 99°F during the next eight hours The temperature regulating center is not completely developed in infants even at term Infants have little body fat and therefore are prone to lose heat by conduction and convection The mechanism for perspiration is not completely developed Infants, therefore, do not perspire as freely as adults and body temperature, as a result, is more labile Hypothermia is deliberately induced for certain types of surgery for infants and children to reduce metabolic rate when oxygenation is a problem This procedure is employed for surgery for correction of congenital heart defects The sub normal temperatures, often as low as 80° F, are withstood better by infants and children than by adults As a matter of fact above the age of 10, it is questionable whether hypothermia should be used as an adjunct to surgery

The trachea of children differs, not only in size, but in contour, from that

of the adult The technique of endotracheal anesthesia must be modified to meet these variations In infants and children the larynx is situated more cephalad than in the adult The diameter of the trachea is smaller, the pharynx is smaller The epiglottis is longer, stiffer and tends to be U or V shaped In the case of the adult it is flat The epiglottis in the infant is inclined at an angle of approximately 45° while in the adult it lies closer and more parallel to the base of the tongue In the infant the hyoid bone is closely attached to the thyroid cartilage, in the adult the structures are farther apart This proximity of the hyoid bone to the larynx causes the base of the tongue to depress the epiglottis so that it protrudes farther into the pharynx All these factors require that laryngoscopes, endotracheal catheters and fittings be small to be adaptable for children of different sizes Catheters must be as thin walled as possible so that they obliterate as little of the cross sectional area of the trachea as possible



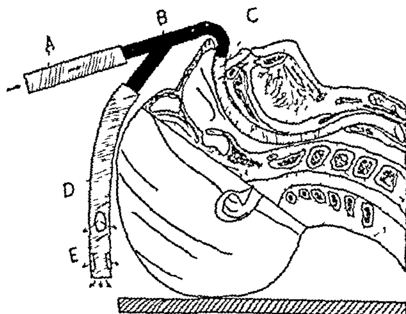
a

Fig 32 Equipment used for pediatric anesthesia a The circle filter modified for pediatric use The dead space in the fittings to the mask has been minimized by placing an inner tube in the connector so that the gases are directed to the mouth of the mask They return in the outer tube on exhalation Rebreathing invariably occurs in the mask but the wash out bulb interposed between the mask and the breathing bag allows fresh gas to be pumped periodically into the mask The breathing bag and the valves on the apparatus have been reduced in size to eliminate resistance

## TYPES OF ANESTHESIA FOR INFANTS AND CHILDREN

It has been and still is a practice for surgeons to use no anesthesia for surgery of infants, particularly the new born The patient is strapped to a cross board and allowed to suck a nipple containing sugar moistened with whiskey This is a barbaric custom Not only does the baby cry in protest during surgery but reflexes are not abolished and the baby squirms about and handicaps the surgeon In addition secretions collect in the pharynx and cause coughing and respiratory obstruction Laryngeal spasm and aspiration are frequent occurrences Death from asphyxia has occurred under such circumstances Developments in pediatric anesthesia are such that the use of this technique is no longer justified

It is taught and it is widely accepted to be a fact that open drop ether is the best type of general anesthesia for pediatric surgery This statement is not correct, however An inhalation anesthetic skillfully administered with a "machine" of the proper design is superior to any by the open techniques There is no doubt that most pediatric anesthesia is performed with open ether This widespread use of open drop ether is due primarily to lack of suitable apparatus The apparatus ordinarily used for inhalation anesthesia for adults has excessive dead space Not only does rebreathing occur when it is used for infants but the proper amount of anesthetic is not delivered into the alveoli Apparatuses having minimal resistance and dead space are not as yet universally available and until they are one must be content with the less satisfactory open methods (Fig 32) One of the objections to open drop ether irrespective of whether it is used for adults or children is the




b

b The insufflation technique described by Ayre The gases are deliverable under slight positive pressure through tube (A) which is connected to (B) the "Y" piece which communicates with (C) the nasal airway (D) A short exhalation and rebreathing tube at the front end (E) Perforations fo the escape of exhaled and excess gases

formation of excess secretions Secretions are more serious and troublesome in infants and children than in adults because, in any event, they cause respiratory obstruction

Clinical experience has shown that children tolerate ether as well as adults There is little doubt that ether is the safest of the inhalation anesthetics for pediatric surgery Difficulties with ether are largely due to improper administration Efforts are now being directed towards improvements in techniques of administration As is the case with ether there is no objection to the use of cyclopropane for pediatric anesthesia if proper apparatus is available for its administration and a skilled administrator undertakes the task The assertion that cyclopropane is contraindicated in infants and children has no scientific basis This belief has been perpetuated because difficulties have arisen when the drug was administered with improper apparatus by unskilled persons who were not familiar with its behavior and peculiarities In the hands of skilled administrators with proper equipment the drug is a most useful one for pediatric anesthesia In the hands of the inexpert, cyclopropane, as in the case of any potent drug is dangerous

Cyclopropane is suited particularly for short surgical procedures or as an induction agent for ether administered by "machine" Ether administered by the closed method may be preceded by ethylene, nitrous oxide or cyclopropane as induction agents There is no objection to the use of nitrous oxide or ethylene for pediatric anesthesia provided non asphyxial concentrations are used As in the case of adults, asphyxia is the chief danger Ethyl chloride has been widely used for minor surgical procedures in pediatric anesthesia Its cardiac effects are well known and cannot be ignored The use of the drug is not advised for any purpose in anesthesia The use of chloroform is not advised for similar reasons

Analgesia with trichlorethylene may be suitable for minor procedures such as changing of dressings, incision and drainages, removal of casts, venepuncture and so on Depth must be confined to stage I or the upper border of stage II, but never any deeper Trichlorethylene may be used to fortify nitrous oxide

The pharmacologic responses of infants and children to non volatile central nervous system depressants is more variable, and less predictable than that of adults In some cases it is not unusual to find they tolerate larger than recommended dosages In others there is less tolerance Larger doses of avertin for example 80 to 100 mgm per kilogram instead of 60 to 80 are required for children than adults The same is true of the narcotics such as morphine, meperidine, methadon and so on Perhaps this is due to the higher metabolic rate infants and children manifest Avertin is suitable as a basal narcotic when administered by rectum The ultra short acting barbiturates may also be used for basal narcosis The rectal administration of thiopental is recommended rather than the intravenous in infants and

children because it obviates venepuncture However if a suitable vein is accessible or has been cannulated for administration of fluids there is no objection to its intravenous use The often made statement that thiopental should not be used in patients below the age of 10 has no scientific basis Thiopental may be used at any age if used with discretion Except for certain difficult intubations a skillful anesthetist rarely needs a muscle relaxant for pediatric surgical patients

From a psychic standpoint, if from no other, children are poor subjects for regional anesthesia It is difficult to predict which child will or will not respond favorably to the use of nerve blocking or infiltration Except for minor surgical procedures, and then only in obviously cooperative subjects, the use of local anesthesia is not advised Spinal anesthesia is not desirable for children for several reasons (1) Children are not psychically suited to undergo surgery while awake (2) Lumbar puncture and intrathecal instillation of drugs is not as simple and as innocuous a procedure as has been surmised, particularly in children (3) The position of the cord is variable and the possibility of trauma to the cord is greater in a child than in the adult (4) The blood pressure is more labile in children than in adults Circulatory derangements are more difficult to control in children (5) In children the degree of relaxation necessary for major surgery can be easily obtained with most general anesthetics Spinal anesthesia is not necessary for relaxation

TABLE XIII
TABLE OF DOSAGES OF DRUGS FOR PREMEDICATION FOR CHILDREN FOR PEDIATRIC ANESTHESIA

| Age | Weight Pounds | Morphine Grains | Morphine Dilutions Dose—1 cc | Scopolamine Grains | Hyoscyamine Grains |
|---|---|---|---|---|---|
| 2 mos | 7–10 | 1/480 | gr 1/12 in 40 cc $H_2O$ | 1/600 | 1/500 |
| 2– 3 mos | 10–12 | 1/360 | gr 1/12 in 30 cc | 1/600 | 1/500 |
| 3– 4 mos | 12–14 | 1/240 | gr 1/12 in 20 cc | 1/600 | 1/500 |
| 4– 7 mos | 14–16 | 1/144 | gr 1/12 in 12 cc | 1/600 | 1/500 |
| 7–11 mos | 16–19 | 1/120 | gr 1/12 in 10 cc | 1/600 | 1/500 |
| 11–18 mos | 19–24 | 1/108 | gr 1/12 in 9 cc | 1/600 | 1/500 |
| 18 mos–2 years | 24–27 | 1/72 | gr 1/12 in 6 cc | 1/450 | 1/250 |
| 2– 3 years | 27–30 | 1/60 | gr 1/12 in 5 cc | 1/450 | 1/250 |
| 3– 5 years | 30–40 | 1/48 | gr 1/12 in 4 cc | 1/450 | 1/250 |
| 5– 8 years | 40–55 | 1/36 | gr 1/12 in 3 cc | 1/300 | 1/175 |
| 8–10 years | 55–65 | 1/24 | gr 1/12 in 2 cc | 1/300 | 1/125 |
| 10–12 years | 65–80 | 1/18 | gr 1/12 in 1 5 cc | 1/200 | 1/125 |

## PREMEDICATION IN CHILDREN

Adequate premedication is more essential in children than in adults if one is to avoid psychic trauma Dosage is difficult to outline empirically because of the variability of response of children to hypnotic and narcotic drugs The response to narcotics varies considerably from one child to the next Attempts have been made to estimate dosage on a milligram per pound basis Such a scheme excludes age which is an important factor A child five years of age may weigh as much as one of 10 but metabolic responses are different in each individual Nevertheless the dose, if given according to weight would be the same for each Obviously the response would be different On the other hand, if dosage is estimated without reference to weight, and only age is considered, the same difficulties arise A larger child tolerates more of the chosen drug than a smaller one of the same age Tables of dosages are available as a general guide (Table VIII) The results are so variable and the effects are not always predictable Premedication in children, even when administered by those expert in the field of pediatric medicine is often guess work

## ENDOTRACHEAL ANESTHESIA

It is advisable to avoid endotracheal anesthesia in infants and children unless it is absolutely necessary However situations do arise in which endotracheal anesthesia is mandatory In neurosurgery, head and neck surgery, thoracic surgery, or surgery performed in the prone position, it is absolutely mandatory One must be prepared to perform a tracheotomy in the event laryngeal edema or tracheitis develops postoperatively One of the drawbacks to endotracheal anesthesia for pediatric surgery and the cause of most difficulties has been the lack of proper equipment The catheters and laryngoscopes cause undue trauma Trauma can be minimized by proper technique As improvements are made in endotracheal apparatus and as satisfactory equipment becomes available endotracheal anesthesia will be used more and more for pediatric surgery Cleanliness has been stressed as an important factor in reducing the post anesthetic morbidity after endotracheal anesthesia Sterility of catheters and laryngoscopes has been stressed as important However, even in the hands of the most meticulous, trauma to the larynx occasionally occurs and laryngeal edema develops

### REFERENCES


ADRIANI JOHN GRIGGS T and BERSON W Aids to pediatric anesthesia *Anesth & Analg 32* 340–349 1953

ADRIANI JOHN and GRIGGS T Rebreathing in pediatric anesthesia *Anesthesiology, 14* 337–347 1953

BAIRD J W Geriatrics and anesthesia *Anesthesiology 4* 17–24 1943

FOLDES F F Some problems of geriatric anesthesia *Anesthesiology 11* 737 744 1950

GROSS R E and FERGUSON C C Surgery in premature babies *Surg Gyn & Obs 95* 631 1952

LEIGH M D BELTON M K *Pediatric Anesthesia* New York Macmillan 1949

STEPHEN R *Elements of Pediatric Anesthesia* Springfield Thomas in Press

# PART III

# RELATIONSHIP OF ANESTHESIA TO TYPE OF OPERATION

## XXIX

# OPERATIONS ABOUT THE HEAD

## INTRACRANIAL OPERATIONS

*Craniotomy* is usually performed for excision of neoplasms, incision and drainage of abscesses due to suppuration, removal of vascular lesions (aneurysms) or debridement for traumatic conditions such as lacerations of the brain, evacuation of hematomas and so on They are also performed for correction of conditions which cause disturbances in formation or drainage of cerebral spinal fluid Patients for craniotomy are apt to be comatose, irrational, psychotic, uncooperative, dehydrated, emaciated or show other manifestations of chronic illness It is not uncommon for signs of increased intracranial pressure to be evident Some have respiratory failure due to medullary depression caused by a lesion, increased pressure or vascular disturbances in the medulla Artificial respiration may be necessary during and after operation

As a rule craniotomies are long operations requiring many hours for completion The surgeon is forced to employ a high frequency coagulating current to secure hemostasis This creates an explosion hazard and precludes the use of flammable anesthetics Frequently excessive bleeding is encountered during surgery particularly when highly vascular lesions are present Most surgeons employ the supine position Some operations, notably posterior fossa explorations (cerebellar), are performed with the patient in the prone position with the head flexed Resections of cranial nerves are often performed with the patient in the sitting position An endotracheal tube is necessary at all times during intracranial surgery when general anesthesia is used It is the only safe means of having complete control of the airway when the patient is unconscious

The scalp is highly vascular When local anesthesia is used epinephrine is added to retard absorption of the local anesthetic drug General anesthesia for craniotomy need be just deep enough to abolish superficial reflexes because muscular relaxation is not necessary The anesthetist must maintain an adequate depth of anesthesia to prevent the patient from straining or coughing because this elevates the intracranial pressure and causes the brain to bulge from the cranial flap Carbon dioxide excess and anoxia also cause the intracranial pressure to rise In certain cases the surgeon prefers to have the patient conscious particularly in situations where stimulation of the motor areas of the brain is part of the procedure Conscious patients being operated upon with local anesthesia complain bitterly of pain as the skull is entered because the periosteum is sensitive and difficult to anesthetize

Projectile vomiting may occur in patients who have brain tumors This increases the possibility of aspiration during the procedure Circulatory and respiratory disturbances may occur reflexly from stimulating certain areas of the brain Convulsions due to the neurologic lesion may occur as anesthesia is induced or during the operation

Local anesthesia is selected if the patient is suited for it When the patient is not suited for it a basal, of an ultra short acting barbiturate combined with nitrous oxide intratracheally is practically mandatory from the standpoint of avoiding fire hazards Straining and coughing caused by the endotracheal tube during light anesthesia is obviated by instilling a topical anesthesic into the trachea The combination of nitrous oxide, ether and oxygen is suitable where one is justified in using a flammable anesthetic in the presence of a fire hazard Ethylene or cyclopropane are not used because of the explosion hazard The use of thiopental alone is not advised because it fails to abolish the superficial and laryngeal reflexes Large quantities are necessary to abolish reflex responses to pain completely Avertin alone is not suitable for the same reasons Some neurosurgeons prefer a combination of avertin and local anesthesia The anesthetist does not have complete control of the airway under such circumstances Besides the operation invariably outlasts the narcosis The anesthetist is then compelled to administer ether or some other general anesthetic under trying circumstances without benefit of an adequate airway

*Trephines* are relatively short procedures performed for diagnosis or for decompression, as a rule Patients are comatose more often than not Local anesthesia is usually satisfactory for these and is the usual choice When not, the choice and management is the same as for craniotomy

*Ventriculograms,* also, are usually performed for diagnostic purposes *Local anesthesia is used unless the patient is not cooperative Under such* circumstances the selection and management is similar to that for craniotomy

*Drainage of brain abscesses* necessitates "turning a flap" and is, therefore, managed in the same manner as intracranial operations Operations such as *lobotomy* may be performed with local anesthesia If local anesthesia is not suitable the procedure is the same as outlined for craniotomy *Resections of the fifth* and other cranial nerves may be performed using local anesthesia If general anesthesia is desired intratracheal nitrous oxide combined with a basal of an ultra short acting barbiturate is preferred An endotracheal catheter is necessary because these operations are usually performed with the patient in the upright position The anesthetist may thus remain at a position distal to the operative field

*Encephalograms* for diagnostic purposes are frequently performed without any anesthetic by some neurologists The procedure is not as innocuous as is believed The patient experiences headache, nausea and vomiting, and other

manifestations of discomfort during and after the procedure Shock and convulsions are some of the more serious sequelae These procedures are usually performed with the patient in the sitting position X ray equipment is necessary so that a fire hazard is created Basal narcosis with thiopental or avertin combined with nitrous oxide anesthesia is satisfactory in most circumstances If basal narcosis alone is used the patient squirms about, struggles and cannot be maintained in a fixed position It is more satisfactory to combine analgesia with the basal narcosis In infants and small children ether is often used Usually the open drop technique is employed This is not always satisfactory because secretions are excessive and ether cannot be safely administered while the X ray examination is in progress Besides, in so many cases the X ray examination room is located at a distance from the anesthetic room, and suction apparatus and resuscitative equipment are not available to the anesthetist

## EXTRA-CRANIAL PROCEDURES

Extra cranial operations range from *removal of cysts* to extensive *plastic operations* of the scalp or cranial vault Selection of anesthesia depends upon the extent and gravity of the contemplated procedure Brief, minor procedures may be performed using local anesthesia When the procedure is extensive and general anesthesia is indicated and the electro surgical unit is not used, cyclopropane intratracheally is ideal If cyclopropane is contraindicated, ether preceded by nitrous oxide or ethylene is satisfactory When a fire hazard exists nitrous oxide intratracheally with a basal of thiopental is used Topical anesthesia and a muscle relaxant are used for intubation The anesthetist must be removed from the operative field in all operations about the head to facilitate surgery This makes the use of an endotracheal catheter mandatory It is not uncommon for some surgeons to attempt surgery with general anesthesia without using an endotracheal catheter in these situations Such a practice is hazardous and occasionally leads to death from asphyxia

### The Eye

Patients requiring surgery of the eye as a rule are very young or beyond middle age In children *muscle imbalance* is the most frequent condition encountered requiring surgery In the older of patients *corneal operations, removal of cataracts* or correction of *glaucoma* are the most frequent procedures Injury to the eye from trauma is a frequent cause of operative intervention in any age group but occurs more often in the young and the middle aged In most eye surgery fixation of the eyeballs both during and after operation is necessary Postoperative nausea and vomiting must be avoided because this frequently induces hemorrhage, thrombosis and other complications which nullify the effect of the operation

Projectile vomiting may occur in patients who have brain tumors This increases the possibility of aspiration during the procedure Circulatory and respiratory disturbances may occur reflexly from stimulating certain areas of the brain Convulsions due to the neurologic lesion may occur as anesthesia is induced or during the operation

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*Encephalograms* for diagnostic purposes are frequently performed without any anesthetic by some neurologists The procedure is not as innocuous as is believed The patient experiences headache, nausea and vomiting, and other

tive in nature and are performed for cosmetic reasons rather than for conditions which may jeopardize life The importance of safe anesthesia cannot be over emphasized Little or no relaxation is necessary from a surgical standpoint The anesthetist must be situated at a point distal to the operative field however Consequently in order to properly maintain an adequate airway during anesthesia an endotracheal catheter must be used

The electro surgical unit may be used by some surgeons in cases where hemostasis is difficult to secure Obviously, this further complicates the selection of anesthesia by creating a fire hazard Many of these operations, since they are simple and of a minor nature, may be performed using local anesthesia Cyclopropane intratracheally is the most desirable choice when general anesthesia is required The rapid induction, its ease and maintenance and the rapid recovery make it ideal for this type of surgery If cyclopropane is contraindicated ether may be used When the electro surgical unit is used a basal of thiopental combined with nitrous oxide is used Topical anesthesia and a muscle relaxant facilitates intubation Ether intratracheally preceded by nitrous oxide or ethylene may be used when the forementioned are contraindicated The disagreeable aspects of ether such as nausea, and emergence delerium must be borne in mind Regional anesthesia obtained by blocking branches of the fifth nerve may be used However, overlapping of this nerve with branches of the cervical plexus in certain areas of the face is not uncommon A block of a single nerve is usually not satisfactory

*Reduction of depressed fractures* of the malar bones are frequently performed by making an incision over the face Local anesthesia is usually satisfactory for these When general anesthesia is desired endotracheal cyclopropane is ideal The other aforementioned choices may be made when cyclopropane is contraindicated

Anesthesia for operations about the *nose, lips, chin, forehead,* and *ears* is selected and managed in the same manner as that for operations about the face

When children are anesthetized for surgery about the face cyclopropane or ether intratracheally with basal narcosis may be used Local anesthesia obviously is a poor choice for children because the psychic make up precludes its use Some surgeons for no obviously sound reasons object to endotracheal catheters and prefer insufflation or open drop ether in these cases The danger of obstruction and death from asphyxia is ever present Unless the operation is brief and one is assured of an excellent airway, omission of the endotracheal catheter for these procedures is hazardous and not advised

## Salivary Glands

Operations on the salivary glands, particularly the parotid, require the same type of anesthesia as for other operations on the face The approach

Most surgery of the eye may be performed using local anesthesia induced by retrobulbar injection and combined with topical application of a local anesthetic drug on the conjunctiva and the cornea When this is not satisfactory cyclopropane intratracheally, combined with a muscle relaxant, may be used As in the case of intracranial surgery, the anesthetist must place himself at a point distant to the operative field The use of an endotracheal catheter, therefore, is mandatory if the airway is to be under control A basal of an ultra short acting barbiturate intravenously minimizes nausea postoperatively Nitrous oxide combined with thiopental and topical anesthesia may be used also The anesthetist must be alert at all times and not allow anesthesia to lighten, otherwise the patient reacts upon the catheter by coughing and straining Such reactions not only interfere with the surgery but initiate complications detrimental to the outcome of a successful operation

The use of thiopental alone, without a supplementary anesthestic and without an endotracheal airway, frequently leads to straining, coughing and sneezing Operations upon the cornea, sclera and other parts of the eye are impossible to perform under such circumstances This technique is also not advised because of the possibility of asphyxia Whenever basal narcosis alone is used the reflex activity which results from stimulation of the cornea may be abolished by the use of a topical anesthetic From the standpoint of surgery intratracheal ether is satisfactory It has the disadvantage of causing nausea, vomiting, struggling and prolonged somnolence in the postoperative period It frequently must be selected when other anesthetics are contraindicated Some ophthalmologists prefer to combine a muscle relaxant with local anesthesia by infiltration The use of this technique is objectionable because the airway is not under the complete control of the anesthetist Others use ether by insufflation without an endotracheal catheter after induction with open drop ether This technique is primitive and not recommended for various reasons, foremost of which is the fact that it is impossible for the anesthetist to have complete control of the airway under such circumstances The head, face, mouth and nose are covered with the drapes necessary for this type of surgery Fatalities due to obstruction and overdosage are more common than is realized Endotracheal ether or cyclopropane is the most common choice for eye surgery for children

## The Face

Most operations about the face are performed for *plastic reconstructions, removal of moles, growths, incisions and drainage* and related procedures The face is a highly vascular area The surgeon may spend considerable time securing hemostasis Plastic operations on the face are usually lengthy and invariably require meticulousness and care The surgeon must work unimpeded and without duress Many operations about the face are elec

### Fenestration Operation

The fenestration operation is an elective procedure which requires considerable meticulousness on the part of the surgeon. The success of the operation depends upon proper hemostasis. The anesthetic techniques described for mastoidectomy are also suitable for these operations. Most surgeons prefer a basal of thiopental or other barbiturate combined with nitrous oxide. Heavy sedation is often used to secure a lowering of blood pressure, to obviate the bleeding which the operator fears. Deliberately induced hypotension with ganglionic blocking agents may have a place in this procedure, if induced for a brief period of time.

### Myringotomy

Myringotomy is most often performed in children although abscesses in the middle ear may occur at any age. The operation requires, at the most, several minutes. Unless the patient is obese or has some deformity of the upper air passages, the anesthetist, as a rule, has good control of the airway. Cyclopropane administered with a mask, without an endotracheal catheter, is suitable, particularly, if an acute respiratory infection is present. Thiopental is less desirable because laryngeal spasm may occur, particularly in patients who have a respiratory infection. Vinyl ether by the open drop method serves admirably for children. Trichlorethylene analgesia may also be used. Ethyl chloride is used by some pediatricians and otologists. The danger of cardiac arrest is ever present. The use of the drug is not advised. Chloroform may also be used but the cardiac effects, likewise, preclude its use. In the event cyclopropane or vinyl ether are not available, open drop ether may be used. However, nausea, vomiting, salivation, prolonged second stage and other objectionable features make its use undesirable.

## The Lip

Operations on the lip are usually performed for excision of growths, correction of a deformity, or incision and drainage of abscesses. *Suture of a hairlip* is frequently performed in children. Some surgeons attempt repairs shortly after birth. Other operations about the lip are performed for excisions of neoplasms, or correction of deformities resulting from trauma. Neoplasms are usually encountered in adults. Most operations in this area are elective. The patients are usually good risks. Oral sepsis, in the adults particularly, may be a factor which causes respiratory complications later. Precautions must be taken during operation to avoid aspiration of blood and secretions which might fall backward into the posterior pharynx. If the lesion extends into the mouth, relaxation of the jaw is required so that the mouth may be opened for introduction of retractors and proper exposure. Certain of these operations are long, others are short. Inasmuch as the anesthetist and the surgeon both compete for the operative field, an endotracheal catheter is required

is from the face rather than through the mouth The presence of the facial nerve in the area of the parotid gland makes these operations tedious and, often times, long General anesthesia, using an endotracheal catheter, is the best choice under these circumstances Local anesthesia is seldom satis factory if the operation is of any consequence Cyclopropane, nitrous oxide, combined with basal of thiopental, or ether may be used

## The Ear

The most common operations otologists perform are mastoidectomy, the fenestration operation and myringotomy Each of these require some form of general anesthesia

### Mastoidectomy

Patients undergoing mastoidectomy are usually young adults or children They may have an acute, or a subsiding, respiratory infection which has precipitated the mastoiditis Signs of sepsis, fever or leukocytosis may be present Meningeal irritation and increased intracranial pressure may be present if there has been extension of the infection Respiration may be depressed as a result of the increased intracranial pressure if extension of the infection to the brain has occurred The operation itself is usually long and tedious, requiring anywhere from two to three hours in the hands of most operators

Anesthesia for mastoidectomy need not be deep as no relaxation is required Some surgeons instill epinephrine in the wound to secure hemo stasis This precludes the use of cyclopropane Some surgeons prefer to use a dental drill for exposing the involved structures The electric motor in this apparatus creates a fire hazard which precludes the use of flammable anesthetics unless, it is explosion proof It usually is not The airway is not under direct control of the anesthetist unless an endotracheal catheter is used The catheter must be used even if there is infection in the upper respiratory tract Cyclopropane intratracheally is ideal for this type of surgery because it is labile non irritating, particularly in the presence of respiratory infections, rapid acting and is followed by rapid recovery Nitrous oxide intratracheally with basal narcosis preceded by topical anes thesia, is the usual choice if a fire hazard exists Nitrous oxide or ethylene followed by ether may be used when cyclopropane or the nitrous oxide combination is not desired Little difference exists between the anesthetic management of children and adults Local anesthesia is not suitable for surgery for either group It is not uncommon for anesthetists to use open drop ether followed by insufflation for mastoidectomy in children The chief objection to this technique is that the airway is not under adequate control This might be justified in small children and infants because the trauma resulting from endotracheal intubation may cause laryngeal edema, but maximum safety is insured by intubation

manipulations An endotracheal catheter is required both to maintain the airway and to permit the anesthetist to remain at a distance from the operative field Many procedures are long and may be attended by considerable blood loss Induction of inhalation anesthesia may often be difficult In many cases the mouth cannot be opened because the joint is fused or the teeth are wired together Oral intubation is difficult or impossible, and a nasal catheter must be used In many cases the face and lower jaw are tender and painful, swollen and edematous precluding the use of a mask

Anesthesia is simplified if the patient is intubated awake using topical anesthesia After the catheter is in place cyclopropane or ether or a combination of the two may be used if one chooses If these are contraindicated, nitrous oxide, combined with a basal of thiopental, may be used Local or block anesthesia is rarely satisfactory and is not recommended In the postoperative period the jaws are often wired together for fixation Respiratory obstruction may occur at the conclusion of the operation when the catheter is removed It is desirable to have the patient react from anesthesia in the operating room so that the retching and vomiting can be cared for at that time For this reason cyclopropane is preferred because it is labile Its depth may be varied at will and rapid recovery is permitted The choice and conduct of anesthesia for children differs little from that for adults An endotracheal catheter is necessary to assure an adequate airway The insufflation of ether, though frequently used, is not safe because the airway is not under adequate control

## The Maxilla

*Resections* of the upper jaw and maxilla are performed to eradicate infections, to correct deformities and injuries and to remove neoplasms Such operations are usually long, time consuming, bloody and traumatic The structures traversed are highly vascular Bleeding can be controlled most effectively by electrocoagulation A fire hazard is thereby created In some instances the blood loss may be so great that it is advisable to deliberately induce hypotension with a ganglionic blocking agent to minimize oozing During the operation blood and secretions may pass into the nasopharynx, inasmuch as the surgical site includes the mouth and the nasal passages or both Frequently, in anticipation of respiratory obstruction during operation, a tracheotomy is performed, prophylactically, prior to the operation under local anesthesia This is highly desirable and simplifies induction and maintenance of anesthesia The apparatus is then connected directly to the tracheotomy tube

When a tracheotomy is not done the use of an endotracheal catheter is mandatory Often the lesion is of such a nature that the mask cannot be applied to the face Under these circumstances the patient is intubated awake, using topical anesthesia General anesthesia is then conducted in the usual manner If electrocoagulation is used, the choice of anesthesia is

to assure control of the airway and still permit the anesthetist to be at a distance In most instances the nasal catheter is preferred to the oral, although the latter may be used if the nasal cannot be introduced

Many operations upon the lip and gums are easily performed using local anesthesia If local anesthesia is not suitable, cyclopropane intratracheally, ether or nitrous oxide combined with a basal of thiopental may be used Topical anesthesia and muscle relaxants may be used to facilitate the intubation Insufflation of ether, particularly in children is often used However this is hazardous because the anesthetist does not have the desired control of the airway and cannot prevent aspiration of blood and secretions into the trachea Nerve locks are usually not satisfactory because there is overlapping between the branches of the trigeminal and cervical nerves in this area

## The Mouth

Operations in the mouth may involve the tongue, the palate, the gums, soft palate and fauces Oral sepsis is often present when the lesions are in the mouth The surgeon, obviously, must have access to the mouth Relaxation is required, so that the mouth may be opened and a gag inserted Many oral operations are lengthy Blood and secretions may be aspirated unless pharyngeal packs are used to prevent secretions from passing into the pharynx In general the choice and conduct of anesthesia is identical to that recommended for operations on the lip

### Palate

Cleft palate is a congenital defect which is usually repaired in early infancy In many cases a feeding problem exists and the operation is performed immediately after birth Otherwise the operation is deferred until the child is a year or two old Maintenance of the airway is the most difficult problem Endotracheal anesthesia is the most desirable choice Usually ether by insufflation is used (Fig 4, p 21) Some anesthetists do not take advantage of the endotracheal catheter and prefer oral insufflation Obviously the airway is not under adequate control under these circumstances Closed system anesthesia may be used if suitable apparatus is on hand

The operation may be performed on adults using nasal endotracheal anesthesia maintained with cyclopropane or nitrous oxide ether sequence or thiopental nitrous oxide Local infiltration or nerve blocks are not satisfactory

## The Mandible

The most common operations on the mandible involve reduction of fractures, correction of deformities, resection of entire or portions of the mandible for tumors, and curettage for osteomyelitis Occasionally, *arthroplasty* or *resection of the temporomandibular* joint is performed for fusion or fixation of the joint Obviously, many of these operations require intraoral

manipulations An endotracheal catheter is required both to maintain the airway and to permit the anesthetist to remain at a distance from the operative field Many procedures are long and may be attended by considerable blood loss Induction of inhalation anesthesia may often be difficult In many cases the mouth cannot be opened because the joint is fused or the teeth are wired together Oral intubation is difficult or impossible, and a nasal catheter must be used In many cases the face and lower jaw are tender and painful, swollen and edematous precluding the use of a mask

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nitrous oxide combined with a basal of thiopental When flammability is no problem, cyclopropane is ideal for this type of surgery Ether, preceded by ethylene or nitrous oxide, may be used when the others are contraindicated Nerve blocks are not satisfactory as a rule because of the overlapping of the cervical and trigeminal nerves The muscle relaxants are useful to facilitate intubation

## Teeth

Most *dental extractions* are office procedures Block anesthesia is the best for office use for exodontia The more complex and extensive extractions may be performed in a hospital, rather than in the office The most common and generally speaking, satisfactory way of conducting general anesthesia in the office for simple extractions, is to administer nitrous oxide fortified with vinyl ether with a nasal mask using the demand type of apparatus (McKesson) Nitrous oxide alone is not satisfactory because it must be given in asphyxial concentrations Of course, the anesthetist does not always have adequate control of the airway using this technique Nitrous oxide, fortified with trichlorethylene, is satisfactorily used by certain anesthesiologists

For more complex and extensive extractions block anesthesia may not be satisfactory and general anesthesia is necessary The jaw must be relaxed for this type of surgery The surgeon must have access of the mouth and the anesthetist of the head A nasal endotracheal tube is thus necessary so that the anesthetist may have adequate control of the airway and be out of the operative field Oral sepsis may be present Lung abscess and other pulmonary suppuration can occur from aspiration of infected material The anesthetist therefore must see that secretions and blood do not pass backward into the pharynx and trachea Cyclopropane is ideal for this type of surgery Nitrous oxide combined with a basal of thiopental, is also satisfactory Ether is a less desirable choice and only used when the other two possibilities mentioned are contraindicated The after effects often are unpleasant

Extraction of deciduous teeth in children may be accomplished by using open drop ether or open drop vinyl ether Nitrous oxide, fortified with vinyl ether used in the same manner as for adults is a better choice If one chooses trichlorethylene may be substituted for the vinyl ether to fortify the nitrous oxide Mixtures of trichlorethylene and nitrous oxide are not flammable Cyclopropane or ether intratracheally is preferred for the longer more extensive operations for both children and adults Ether by insufflation is still used by some anesthetists for these extensive extractions Lack of control of the airway is an objectionable feature which makes the technique hazardous Thiopental alone is used by many dentists for office surgery under the most adverse circumstances Its use cannot be condoned Sooner or later disaster results

## Sinuses

Operations upon the nasal sinuses involve *antrotomy* for control of infections and removal of new growths Patients requiring antrotomy frequently have a postnasal drainage of purulent or mucoid material It is not uncommon for the nasal passages to be occluded by polyps, bony spurs, and other obstructions in such a manner that a nasal endotracheal catheter cannot be introduced without undue trauma Chronic bronchitis, pharyngitis, laryngitis and cough may be associated with the postnasal drainage Antrotomies are usually lengthy, traumatic and are often accompanied by considerable bleeding The possibility of emboli due to aspiration of air caused by opening venous sinuses must be considered As in other operations about the head the anesthetist must relinquish the surgical field to the surgeon The use of an endotracheal catheter is mandatory if he is to have full control of the airway Less extensive operations may be performed using nerve blocks The sphenopalatine ganglion or branches of the maxillary nerve may be blocked to yield adequate anesthesia Extensive, long operations require general anesthesia, however Cyclopropane is the anesthetic of choice when general anesthesia is indicated When cyclopropane is not desirable or cannot be used nitrous oxide combined with a basal of thiopental may be used If neither choice is desired, ether preceded by ethylene or nitrous oxide may be used The slow recovery, nausea, vomiting and other disagreeable features of ether obviate its use Ether by insufflation is still used extensively but use of this technique is not advised because the anesthetist does not have proper control of the airway

## The Pharynx

The most common intra pharyngeal operations are tonsillectomy and adenoidectomy Other operations include removal of cysts or growths, drainage of abscesses, repair of defects of the hard palate, soft palate and plastic procedures on the fauces They are less common but not necessarily rare

### Tonsillectomy and Adenoidectomy

Patients requiring tonsillectomy are usually children and young adults The lymphoid tissue may be so hypertrophied that it obstructs the airway Inasmuch as the surgeon must have access to the mouth and nasopharynx these operations are best done with an endotracheal catheter in place so that the anesthetist may be out of the operator's way and still have control of the airway Although their duration cannot be postulated, they are usually brief unless hemorrhage complicates the procedure This occurs when one least anticipates it and the operation is then prolonged Relaxation is necessary for introduction of the mouth gag Anesthesia must be of sufficient depth to abolish the gag reflex Local anesthesia is the method of choice and the safest for adults It is without a doubt the best choice if

the patient tolerates it and the operator feels at ease in performing the operation with it

When general anesthesia is desired intratracheal cyclopropane is ideal for tonsillectomy as well as for other pharygeal surgery The catheter is introduced nasally if adenoids are not present and orally if they are Rapid recovery is always assured with cyclopropane One objection to cyclopropane is that increased oozing appears to occur Ether intratracheally is satisfactory but less desirable due to the objectionable post anesthetic effects Recovery is not as rapid with ether as with cyclopropane A basal of thiopental may be used prior to either cyclopropane or ether Postoperative depression of respiration can be avoided by using minimal amounts of the basal A basal of an ultra short acting barbiturate, nitrous oxide intratracheally and a muscle relaxant is also used for tonsillectomy It is less satisfactory than the inhalation anesthetics because of the depression of respiration which follows in the post operative period Ether by insufflation directly into the pharynx is a common method of administering anesthesia for tonsillectomy In adults the concentration of ether necessary to maintain adequate depth of anesthesia is delivered with difficulty The chief objection however, is the difficulty in maintaining the airway with this technique

The insufflation technique is standard for tonsillectomies and adenoidectomies in children Whether or not an endotracheal catheter should be used is controversial Certainly a catheter insures an adequate airway With improvements in apparatus and technique, endotracheal anesthesia is being used more and more for pediatric surgery However, the possibility of trauma to the larynx still exists In children, due to the presence of adenoids, the catheter is placed orally rather than nasally Most otolaryngologists do not object to the oral tube even in adults Ultra short acting barbiturates *alone are not satisfactory for anesthesia for tonsillectomy in adults or* children Large quantities of the drug are needed to abolish reflexes Hypoventilation and the possibility of laryngeal and bronchial spasm are ever present The airway is difficult to maintain safely without an endotracheal tube The barbiturates often initiate bronchial spasm Prolonged somnolence invariably follows the use of large quantities of barbiturates The quantity which may be required is not easily predicted

### Drainage of Peritonsillar and Retropharyngeal Abscess

Anesthesia for drainage of a peritonsillar abscess follows the same general pattern, indications and contraindictions as that recommended for tonsillectomy It is important that the abscess is not ruptured in attempting intubation otherwise aspiration of purulent material may occur Whenever possible local anesthesia should be used When local anesthesia is not satisfactory or cannot be used cyclopropane conducted through a nasal or oral intratracheal catheter, whichever is simpler to introduce, may be used

In children the usual technique employed by most operators is ether by insufflation The possibility of aspiration and asphyxia from lack of control of the airway is always present, however An endotracheal catheter is desirable, even in children

## The Larynx

Laryngeal operations are performed for removal of polyps, or other growths on the vocal cords and cauterizations Removal of the larynx itself for malignant tumors is a formidable but not uncommon procedure Direct vision is required for intralaryngeal surgery Relaxation is necessary The chief difficulty encountered is maintaining an airway On occasions anesthesia is required merely for examination for diagnosis under direct vision

### Laryngectomy

Laryngectomy is performed for carcinoma most often Usually the patients are in good condition General anesthesia is mandatory for this operation Respiratory obstruction and dyspnea may be present if the growth is large If the patient has any difficulty in maintaining an adequate airway preoperatively the situation certainly will not improve during general anesthesia A preliminary tracheotomy is advisable under such circumstances Otherwise the patient may be anesthetized with endotracheal anesthesia in the usual manner As soon as the larynx is extirpated a sterile endotracheal catheter is introduced into the trachea by the surgeon and anesthesia is maintained in the usual manner Inasmuch as both the anesthetist and the surgeon compete for the operative field, an endotracheal tube is mandatory to permit the anesthetist to stand at a distance and still maintain the airway Vago vagal reflexes may arise, initiated by manipulation of the trachea These may be minimized by the use of topical anesthesia and anticholinergic drugs

Cyclopropane is the ideal anesthetic for this procedure If a cautery is used, and it usually is not, nitrous oxide combined with a basal narcosis of thiopental is used If cyclopropane and the nitrous oxide-thiopental combination are contraindicated ether intratracheally may be used Local anesthesia is not satisfactory from both psychic and technical standpoints Few surgeons care to operate under the conditions it offers or are sufficiently skilled to use it Cervical plexus block supplemented by local infiltration would be adequate for this area However, the operation is time consuming and is sure to outlast the block

### Suspension Laryngoscopy and Other Operations

Other laryngeal operations including suspension laryngoscopy are usually best performed with combinations of a basal narcosis of thiopental, topical anesthesia and a muscle relaxant Relaxation is necessary to properly visual

ize the larynx Ether by insufflation has been used for adults for many years It is seldom wholly satisfactory and invariably difficult to manage The concentration of ether necessary for maintenance of adequate depth of anesthesia is difficult to deliver because the method is open

For children open drop ether followed by insufflation appears to be the accepted and most common method used It is neither the best nor the safest, but is the simplest under most circumstances A basal of an ultra short acting barbiturate, or avertin may be used, but laryngeal spasm may result and respiratory depression may follow in the postoperative field This, of course, is undesirable

### Tracheotomy

Tracheotomy is usually performed as an emergency procedure often in desperate situations Obstruction and all the manifestations of asphyxia are usually present and death is eminent Time is a factor and the use of anesthesia is out of the question When the situation is not so desperate or when the tracheotomy is elective it is usually performed using local anesthesia When it is elective and general anesthesia is desired intratracheal cyclopropane, ether, cyclopropane-ether or nitrous oxide with a basal of thiopental may be used for adults and children

## Bronchi

Operations and diagnostic procedures involving the lower trachea and bronchi are performed with endoscopic instruments The approach is through the larynx by means of a bronchoscope The most common procedures performed are securing of a biopsy, visualization of masses or removal of foreign bodies Often suppurative disease or pulmonary insufficiency are complicating factors Coughing and copious secretions are troublesome to both operator and anesthetist Some patients are anemic and emaciated Vagal reflexes may be initiated by this instrumentation but they are not troublesome as a rule Anticholinergic drugs may be used to minimize them Relaxation of the muscles of the jaws and neck is necessary Often these procedures are performed in a dark room which handicaps the anesthetist as far as closely watching the patient is concerned Coughing, bronchial spasm and diminished ventilation follow the induction of anesthesia The airway is not easily maintained A fire hazard exists in view of the fact that these instruments are electrical Bulbs, cables, and switches may be the source of a spark

There is no wholly satisfactory method of managing anesthesia for these procedures Topical anesthesia is the best choice for bronchoscopy wherever it is possible to use it However when the patient is not cooperative, has dyspnea or is apprehensive general anesthesia is the usual choice Thiopental, combined with a muscle relaxant preceded by thorough cocainization is the method employed It must be admitted that this technique has

drawbacks but there is little else from which to choose Open drop ether followed by insufflation is the method usually employed for bronchoscopy for children It may be used for adults also but is far from ideal and not technically simple to manage

### Bronchograms

Bronchograms are diagnostic procedures usually performed on patients who have suppurative disease in the lung It is common for such subjects to be anemic and emaciated and to show signs of sepsis Invariably they have pulmonary dysfunction and cough The procedure consists of introducing a cannula into the trachea through which an oily opaque substance is injected Following injection fluoroscopy is performed in a dark room A fire hazard thus exists Relaxation is necessary for visualization of the larynx for the intubation Introduction of an endotracheal catheter through which the cannula for the oil is passed facilitates the procedure considerably A momentary period of apnea must be induced during which the lung fields must be immobile while the x ray is being taken Coughing, bronchospasm and diminished ventilation and signs of respiratory distress usually follow the injection of the oil

In adults these procedures are usually performed with topical anesthesia using tetracaine or cocaine However, for patients who are not cooperative general anesthesia must be used Nonflammable agents must be used inasmuch as the procedure is done in the vicinity of high frequency equipment A basal of thiopental or avertin combined with nitrous oxide intratracheally (with topical anesthesia) is the usual selection Succinyl choline is used to facilitate intubations Certain anesthetists disregard the explosion hazards and use ether or cyclopropane intratracheally In the fluoroscopic room a changeover is made to thiopental nitrous oxide oxygen Topical anesthesia is not satisfactory for children as a rule The procedure used for adults may be used for them when local anesthesia is feasible Some anesthetists prefer to induce anesthesia with open drop ether and then maintain it by insufflation It must be remembered that vagal reflexes may be initiated by the injection of the contrast media Prophylatic premedication with atropine preanestheti cally is advised Basal narcosis, of course, is undesirable because it causes respiratory depression in the postoperative period Unless topical anesthesia is used to abolish the spasmogenic responses which are enhanced by the thiopental, results will be unsatisfactory

## The Esophagus

Esophagoscopy is mentioned along with bronchoscopy because the problems involved are similar Like bronchoscopy esophagoscopy is performed for diagnostic purposes with endoscopic instruments Many subjects for whom esophagoscopy is performed are emaciated from poor nutrition

because of inability to swallow Neoplasms, persistent spasm of the esophagus, and diverticuli are the common clinical conditions encountered Removal of foreign bodies and the diagnosis of traumatic lesions and functional diseases are other reasons for performing esophagoscopy Local anesthesia is used frequently for esophagoscopy Relaxation and cooperation is required from the patient as for bronchoscopy If topical anesthesia is not satisfactory general anesthesia is necessary Both the surgeon and the anesthetist then compete for the operative field The airway is then difficult to maintain An endotracheal catheter hinders some operators and they therefore request that it be omitted Secretions of mucous, vomiting and retching often occur Vagal reflexes likewise are initiated by passage of the instrument into the esophagus Cyclopropane intratracheally with a muscle relaxant may be used when an endotracheal catheter is introduced Where the catheter is in the operator's way the combination of a basal of thiopental, topical anesthesia and a muscle relaxant may be used The possibility of laryngeal spasm is ever present Ether intratracheally may also be used if cyclopropane is contraindicated For children vinyl ether followed by the open drop ether technique followed by ether by insufflation is the usual method of anesthesia employed It is customary to omit the intratracheal catheter However, a catheter is highly desirable because an adequate airway is assured The combination of a basal of thiopental, topical anesthesia and a muscle relaxant carries a greater degree of hazard in children than in adults and its use is not advised unless there is no other choice

## REFERENCES


ADAMS R. C Regional anesthesia for operations about the upper extremity *Anesthesiology* 2 513–530 1941

DAVIS D Anesthesia for suspension laryngoscopy *Anesthesiology, 11* 245–253 1950

GORDON R. A. Problems of anesthesia for plastic surgery *Anesthesiology, 3* 507–513 1942

LEIGH M. D KESTER, H. A. Endotracheal anesthesia for operations on the cleft lip and cleft palate *Anesthesiology 9* 32–41 1948

MAHEL H. P PON L. H. CHIPS J E Anesthesia in maxillofacial surgery *Anesthesiology 14* 498–500 1953

MOUSEL L. Regional anesthesia for operations about the head and neck *Anesthesiology, 2* 61–74 1941

MEAK W G Anesthesia for fenestration operation *Anesthesiology 9* 644, 1948

HERSHENSEN B B Anesthesia for neurosurgery *New York State J Med 42* 211 1942

PAPPER, E. and HOWLAND W S Circulatory changes during anesthesia for neurosurgical operations *Anesthesiology 13* 343–350 1952

ROCHE, K. T Anesthesia for recent injuries of jaw and face 7 233–254 1946

SLOCUM H C. ALLEN C R. Orotracheal anesthesia for cheilioplasty *Anesthesiology 6* 355–359 1945

TAMERIN J A. DEPOLO E. J Anesthesia for corrective rhinoplasty *Anesthesiology, 13* 94–102 1952

TEPLINSKY L. L. HARNS Z CASSELS W H. *et al* Anesthesia for neurosurgery *Anesthesiology 10* 82–90 1949

# XXX

# OPERATIONS ON THE NECK

## ANTERIOR ASPECT OF THE NECK

### Thyroidectomy

Thyroidectomy for goitre and nodules in the gland is the most frequent operation performed in the neck area The nature of the goitre is important Whether or not it is toxic or non toxic, whether it is cystic or solid, whether or not it compresses the trachea, whether or not it is malignant or benign, whether or not metastasis have extended to other structures of the neck are important factors Toxic goitres may be associated with heart disease Patients for thyroidectomy for removal of toxic goitres are usually apprehensive, highly excitable and have a high metabolic rate Excitement or any emotional strains are to be avoided Vasoconstrictors and other sympathomimetic amines cannot be used for any purposes including local anesthesia for these patients Vocal cord paralysis, edema of the larynx, tracheitis or a deviated trachea are often present The mass in the neck may extend into the thorax Tachycardia, arrhythmias, a low diastolic, a high systolic and a wide pulse pressure are frequently present

Patients who have non toxic goiters and cysts or solitary nodules do not have apprehension, increased cardiac output or a high metabolic rate

Thyroidectomy is best performed using general anesthesia Muscle relaxation is a minor factor in the operation except at time of intubation Anesthesia need not be deeper than second plane as a rule The head is hyperextended to gain exposure, causing the airway to become obstructed The use of an endotracheal catheter is mandatory for thyroidectomy The anesthetist must be out of the surgeon's way since they both compete for the operative field This is further indication for an endotracheal tube Oozing and bleeding are frequent particularly after the use of thiouracil and related antithyroid compounds Excess secretion may be anticipated, particularly when potassium iodide has been used preoperatively In toxic goitres the oxygen consumption and carbon dioxide output are high

Postoperatively the possibility of heat retention, hyperthermia and thyroid crisis are present Postoperative tracheitis from manipulations of the trachea and the use of the endotracheal tubes are common Hematomas developing from inadequate hemostasis may cause respiratory obstruction in the postoperative period The possibility of cardiac failure both during and after operation must be borne in mind Vocal cord paralysis from injury or severance of the recurrent laryngeal nerves is manifested by respiratory

difficulty following removal of the endotracheal tube Collapse of the trachea postoperatively may occur particularly when respiratory obstruction develops in the postoperative period This is said to be due to weakening of the tracheal wall

The choice of anesthetic for toxic goitres is ethylene or nitrous oxide followed by ether intratracheally This is best preceded by basal narcosis induced by heavy doses of morphine and scopolamine, avertin rectally, or intravenous ultra short acting barbiturates Local anesthesia or cervical plexus block are not suitable for patients with toxic goitres, as a rule If used the patients must be heavily sedated because the psychic effects cause tachycardia and disturbances in blood pressure Cyclopropane is avoided by most anesthetists because of its effect on cardiac automaticity

Cyclopropane, ethylene or nitrous oxide followed by ether, local or cervical plexus block may be used for removal of non toxic goitres, cysts or nodules *Thiopental, alone or combined with a muscle relaxant, should* not be used as neither is anesthetic An analgesic substance, preferably nitrous oxide or ethylene should be added It is unwise to attempt thyroidectomy without using an endotracheal catheter because of the possibility of obstruction and asphyxia The anesthetic management for thyroidectomy for children is identical to that of adults

The anesthetic management of excision of *thyroglossal* cysts is the same as for thyroidectomy for non toxic goitres Explorations for removal of *parathyroid tumors* are likewise managed in the same manner Preoperative treatment with calcium and parathyroid extract may be necessary

Dissections for excision of *branchial clefts*, hygromas and other *cysts* of the neck are oftentimes extensive, time consuming and require deep dissection Anesthesia is managed in the same manner as it is for thyroidectomy for non-toxic goitres for both adults and children

## Radical Dissections of the Neck

Anesthesia for radical dissections of the neck for removal of malignant or infected lymph nodes or removal of tumor masses is managed in the same manner as that for thyroidectomy Operations for malignant disease are usually performed in patients in the older age groups The operation is rather long and tedious as a rule No muscle relaxation of any consequence is needed however Inasmuch as the surgeon and anesthetist both compete *for the operative field, the use of an endotracheal catheter is mandatory* to assure a patent airway The carotid sinus may be hyperactive, and if manipulated unduly, circulatory and respiratory disturbances may occur Manipulation of the trachea may result in tracheitis, and bronchial or laryngeal spasm The anesthetic of choice for these procedures is cyclopropane Where cyclopropane is not desired or contraindicated, nitrous oxide or ethylene followed by ether is satisfactory When neither cyclopropane

nor ether is desired or suitable a basal of thiopental combined with nitrous oxide intratracheally and topical anesthesia is used The amount of thiopental must be kept at a minimum otherwise the patient may develop prolonged respiratory depression in the postoperative period The combination of nitrous oxide and thiopental is suitable when the electrosurgical unit is used or other fire hazard exists

## Biopsies, Removal of Cysts, etc

Biopsies, removal of cysts, nodes, etc are usually performed using infiltration of a local anesthetic Local infiltration is suitable for minor procedures only Anything of an extensive nature is managed in the same manner as for thyroidectomy

*Ligations* of the *carotid artery* and *jugular vein* likewise are managed in the same manner as thyroidectomy *Angiograms* and other visualizations of the vascular system of the neck and head are performed under local anesthesia However, when this is not feasible, the management is the same as for thyroidectomy Whenever x-ray apparatus or high frequency units are necessary the combination of a basal of thiopental and intratracheal nitrous oxide is used

The choice of anesthesia for patients for carotid stripping for hyperactive carotid sinus requires special consideration Circulatory disturbances are the rule Bradycardia, syncope or convulsions may be precipitated by manipulation of the carotid vessels Manipulation of the structures on the lateral aspect of the neck must be avoided prior to operation Intratracheal ether or thiopental combined with nitrous oxide intratracheally are preferred to other methods of anesthesia Cyclopropane is less desirable because of its reflex effect on cardiac irritability

## Incision and Drainage of Abscesses

Incision and drainage of abscesses in the neck region presents the problem of maintaining an adequate airway It is the most important single consideration for this type of operation In *Ludwig's angina,* particularly, edema of the pharynx and floor of the mouth may be so diffuse that the patient has obstructive dyspnea The patient must sit up to breathe It is hazardous to use general anesthesia without an endotracheal tube for this type patient The catheter must be placed in the trachea before anesthesia is induced, that is, while the patient is awake Unless an adequate airway is provided before anesthesia is induced the patient will become completely obstructed as soon as he is sufficiently relaxed The voluntary effort which the patient makes while conscious is nullified as soon as unconsciousness supervenes The airway becomes obstructed and the patient promptly dies from asphyxia

When it is not feasible to intubate a patient prior to induction of anes

thesia a tracheotomy should be performed using local infiltration General anesthesia may then be induced through the tracheotomy tube with whatever drug is desired Cyclopropane is ideal for this type of surgery Cervical plexus block of course is contraindicated because of the possibility of spreading the infection Fatalities during this type of surgery are, as a rule, due to asphyxia It must be borne in mind that these infections are often associated with diabetes, leukemia and other systemic diseases Oral sepsis may be present since these abscesses are often complications which follow extraction of the teeth The patient is usually unable to swallow and secretions may accumulate in the mouth which further add to the difficulties of inducing anesthesia

## Posterior Aspect of the Neck

Operations on the posterior aspect of the neck usually consist of *excisions of lipomas, fibromas* and other growths, removal of cysts, *incision and drainage of carbuncles,* abscesses and other suppurative lesions Irrespective of the type of procedure, the surgeon operates with the patient in the prone position Unless local anesthesia is used and this is not always possible, the airway is maintained with difficulty The anesthetist also must be placed at a distance from the surgical field It is mandatory, then, that an endotracheal catheter be used when all such operations are performed using general anesthesia Circulatory derangements may occur as the patient is turned from one position to the other In view of the fact that the neck area is highly vascular some surgeons prefer to use the electrosurgical unit to secure hemostasis A fire hazard is then created under such circumstances

Intratracheal cyclopropane is the ideal choice for this type of surgery If a fire hazard exists nitrous oxide with a basal of thiopental is the usual choice but not necessarily the best one If cyclopropane is contraindicated ether may be used Local anesthesia is satisfactory for the minor procedures Under no circumstances should inhalation or intravenous anesthesia be used without an endotracheal catheter Thiopental alone of course does not provide surgical anesthesia in the true sense and certainly is not desirable The management of anesthesia for this type of surgery is the same for children as for adults

REFERENCES

BENNETT J H Anesthetic management for drainage of abscess of submandibular space *Anesthesiology, 4* 25–30 1943

COVELL, H D Anesthesia for radical neck surgery *Ann West Med & Surg, 2* 457–460 1948

DECOURCY, J L *Pathology and Surgery of the Thyroid Gland* Springfield Thomas 1949

MANSEL L H COAKLEY C S Anesthetic management of patients with thyroid disease *Anesthesiology, 10* 444–450 1949

WOODBRIDGE P D Anesthesia for otolaryngologic surgery Chap from *Diseases of Nose & Throat* by Jackson Saunders, Philadelphia 1945

# XXXI

# INTRA- AND EXTRA-THORACIC OPERATIONS

## OPERATIONS ON THE THORACIC WALL

Operations on the thoracic wall may vary from excisions of simple cysts, lipomas, fibromas, plastic repairs, axillary dissections, removal of lymph nodes and similar procedures No relaxation is required The anesthetist as a rule is far enough removed from the surgical field to have adequate control of the airway An endotracheal tube, therefore, is not required unless the prone or lateral position is employed or when the lesion or site of operation is on the back or at clavicular areas Local infiltration may be used for minor procedures Cyclopropane by the usual technique is ideal when general anesthesia is required Nitrous oxide or ethylene combined with basal narcosis of thiopental may likewise be used When basal narcosis cannot be used and if the patient cannot be maintained with nitrous oxide or ethylene, ether may be added Intercostal or paravertebral blocks may be used if the operative site is in the area supplied by a given thoracic segment The overlapping between the cervical plexus and the upper thoracic nerves precludes the use of intercostal and paravertebral blocks when the operative site is over the shoulder or in the clavicular area

### Mammectomy

Simple mammectomies and radical mammectomies are actually operations on the thoracic wall No relaxation is needed because the gland is really a subcutaneous organ Simple mammectomy may be performed using local anesthesia However the use of local anesthesia is not advised for apprehensive patients When carcinoma is suspected and a radical mammectomy preceded by a biopsy is contemplated the patient should be heavily sedated or should be given a basal of intravenous thiopental, in the event the frozen tissue study is positive Performing the biopsy with local anesthesia and then proceeding with general anesthesia if a radical mammectomy is indicated frequently creates a difficult situation The psychic trauma resulting from the realization that a carcinoma is present and that a radical mammectomy is necessary often is the basis of emotional disturbances in the postoperative period The best plan is to proceed with general anesthesia for both the biopsy and the mammectomy The patient may be maintained under light anesthesia without undue harm while the pathologist is making his examination

Radical mammectomy requires some special considerations by the anesthetist The operation is rather lengthy in most instances, extensive and requires meticulousness It may be accompanied by blood loss and possibly shock

Patients, in the older age group, may have co existing degenerative diseases particularly of the cardiovascular type Anemia or weight loss are observed in advanced cases Some surgeons use a high frequency unit for hemostasis and thereby create a fire hazard

Ordinarily cyclopropane is ideal for radical mammectomies Ethylene or nitrous oxide fortified with ether are likewise satisfactory when cyclopropane is not desired The use of basal narcosis using thiopental or other such barbiturate intravenously prior to inhalation anesthesia is advised When the electro surgical unit is used nitrous oxide combined with a basal of an ultra short acting barbiturate is the most desirable choice An endotracheal catheter is not necessary unless the anesthetist has difficulty in maintaining the airway, as in the case of obese individuals Muscle relaxants are not indicated Local anesthesia is not satisfactory for a radical mammectomy but may be used for simple mammectomies Paravertebral blocks and intercostal blocks are not satisfactory because, as a rule, it is difficult to anesthetize the segments supplying the surgical site

## Thoracoplasty

Although thoracoplasty is an extra pleural operation and involves the chest wall only, it is usually considered an operation of thoracic surgery The physiologic and medical problems involved are common to other operations for chest disease Thoracoplasty is performed most often on patients for chronic pulmonary tuberculosis Less frequently it is performed after pneumonectomy or empyema to collapse the chest wall to obliterate an intra pulmonary cavity or obliterate the pleural space Patients for thoracoplasty may be in any age group but are usually middle aged or young The majority are chronically ill Decreased pulmonary reserve, dyspnea, fever, and weight loss are usually present The presence of tuberculous tracheitis may preclude the use of an endotracheal catheter If a *tracheobronchial cutaneous fistula* is present a closed system of anesthesia is maintained with difficulty even when the opening is sealed Muscle relaxation is not a requisite Thoracoplasties vary in duration depending upon the technical difficulties and the dexterity of the operator They are usually performed in the lateral position A high frequency unit is used by a few surgeons for hemostasis A fire hazard is thereby created

Circulatory depression due to trauma, lateral posture, blood loss and reflex stimulation from manipulations of the ribs and pleura are the rule rather than the exception A fall in blood pressure frequently occurs as the patient is turned from the lateral to the supine position at the conclusion of the operation The etiology of this hypotension still remains to be determined although hypercapnia has been incriminated Carbon dioxide retention due to inadequate ventilation necessitates the use of the closed system and intermittent positive pressure for assisting or controlling respiration

An endotracheal catheter is mandatory for these operations because secretions must be aspirated and an unobstructed airway must be maintained at all costs Thoracoplasty is performed satisfactorily using intratracheal cyclopropane This drug is non irritating, is labile, permits rapid induction, is followed by rapid recovery, is characterized by quiet breathing and provides relaxation for intubation A muscle relaxant preferably succinyl choline may be used to facilitate the intubation Should arrhythmias develop they may be controlled by the addition of ether

If well defined cardiac disease is present ethylene or nitrous oxide followed by ether may be used instead of cyclopropane A cautery is seldom used, but, if it is required, nitrous oxide combined with a basal of an ultra short acting barbiturate may be used although it is far from desirable Topical anesthesia is desirable to facilitate the intubation The possibility of laryngeal spasm, bronchial spasm and respiratory depression in the postoperative period are the objectionable features to this combination Paravertebral block may be used but requires meticulousness on the part of the operator Besides it is not suitable from a psychic standpoint The periosteum is not easily anesthetized, considerable discomfort is felt when the ribs are excised Local anesthesia is not satisfactory for the same reason Peridural block has been advocated but has never enjoyed any popularity As in the case of paravertebral block psychic factors are important considerations Then, the block is not simply induced nor is it satisfactory even in the hands of the most expert The use of spinal anesthesia, although advocated by the bolder and perhaps more reckless anesthetists and surgeons, is not advised Respiratory failure due to intercostal and diaphragmatic paralysis and severe hypotension are common occurrences

Shock, tension pneumothorax, air emboli and respiratory acidosis are some of the complications which occur at the conclusion of and during a thoracoplasty

## INTRA-THORACIC OPERATIONS

Intra-thoracic operations involve the pleura, the lungs, the trachea, the bronchi, the mediastinum and its contents, and the diaphgram

### Operations on the Pleura

Operations involving the pleura are performed for drainage of collections of purulent material, blood or fluid from the pleural space, decortication of fibrous tissue, thickening due to infection and removal of tumors Removal of tumors arising from the pleura entails resection of the chest wall Drainage of the pleural space necessitates resections of ribs Most patients requiring surgery of the pleura are acutely or chronically ill It is not uncommon for them to have signs of sepsis, fever, anemia, decreased pulmonary reserve, cough, dyspnea and orthopnea A bronchopleural or broncho-

pleural cutaneous fistula is present on occasions Often an associated pneumonitis is present

Relaxation is not a factor in drainage of the space or other operations on the pleura The patient is usually placed in the upright sitting position for thoracotomy to facilitate drainage Regional anesthesia, usually para vertebral block, is used The patient is conscious He is easily placed and remains in the upright position Intercostal block is not as satisfactory as paravertebral block for this purpose When general anesthesia is required cyclopropane intratracheally is the most suitable choice because it is non-irritating, allows adequate oxygenation, is characterized by a rapid induc tion and is followed by rapid recovery When cyclopropane is contraindi cated ether preceded by ethylene or nitrous oxide may be used Nitrous oxide combined with a basal of an ultra short acting barbiturate may be used but is not desired because of the spasmogenic nature of the barbiturates and the depression of respiration which follows in the postoperative period

Drainage of an empyema by use of trocar or injection of air into the pleural space is performed with local anesthesia

## Lung

A pneumonectomy may be either partial or complete A partial pneumo nectomy, or lobectomy, as it is called, is more tedious and time consuming than a complete one because the individual vessels, bronchi and other hilar structures must be dissected and identified Partial pneumonectomy is performed for suppurative diseases, removal of foreign bodies, benign tumors or tuberculosis Occasionally a portion of a lung is removed because an existing foreign body cannot be dislodged or removed by bronchoscopy or other techniques Complete pneumonectomy is performed for removal of malignant tumors Pneumonectomy is technically less difficult and meticu lous than lobectomy

Patients undergoing pneumonectomy have diminished pulmonary reserve more often than not When the operation is performed for suppurative diseases sepsis and all its manifestations are usually present Sepsis may also complicate neoplastic diseases if the tumor mass is large and long stand ing Atelectasis is not an uncommon complication If mediastinal nodes are enlarged due to infection or metastasis paralysis of the vocal cord may be present particularly on the left side Inasmuch as the chest is open and pneumothorax is present, assisted or controlled respiration is invariably necessary to maintain proper ventilation Relaxation is not a requisite Many pneumonectomies and almost all lobectomies are performed with the patient in the lateral position Some pneumonectomies may be performed in the supine position This position, of course, simplifies anesthesia and permits adequate ventilation

Some surgeons prefer the prone position for resection of a lobe for tuber-

culosis The prone position often interferes with proper ventilation and makes anesthesia technically difficult Hemorrhage due to inadvertent injury to major vessels is a possibility during pneumonectomy When adhesions are numerous a continuous ooze occurs which is difficult to control Excessive quantities of blood are often lost A fall in blood pressure follows, unless the blood is replaced as it is lost Troublesome secretions are usually present during pneumonectomy which require frequent use of the suction An endotracheal catheter is mandatory to facilitate aspiration of secretions by suctioning, for exerting positive pressure and to prevent coughing Coughing creates an excessive intra thoracic pressure which is undesirable In addition hilar and tracheobronchial reflexes cause laryngeal spasm The laryngeal spasm is prevented by the catheter, but the tracheal and bronchial reflexes are not In positions other than the supine, ventilation is impeded giving rise to both anoxia and carbon dioxide retention Vagal, hilar and tracheobronchial reflexes often cause circulatory disturbances The blood pressure may fall, the pulse may become slow and irregular

Coughing and bronchial spasm are frequent during the induction of anesthesia particularly when suppurative diseases are present These add to the anesthetist's difficulties Hemoptysis, particularly when the patient has bronchiectasis or tuberculosis, has caused death by drowning (asphyxia) during surgery During drainage of a lung abscess the purulent exudate may suddenly gush into a bronchus as the abscess cavity is entered and death from asphyxia swiftly follows The anesthetist is almost helpless in such situations An endobronchial catheter is used instead of an endotracheal when purulent material is excessive Such a tube allows catherization of each bronchus so that secretions do not pass from the diseased lung to the healthy lung In theory the thought is excellent but in actual practice endobronchial anesthesia is difficult to execute and is often impractical

Intratracheal cyclopropane is a most useful drug for most intra thoracic surgery The rapid induction and the rapid recovery are ideal features It is labile, non irritating, permits quiet breathing, and allows adequate oxygenation Ether is added when arrhythmias appear Ether exaggerates respiratory movements due to its local stimulating effect This exaggerated breathing may be annoying to the surgeon and may handicap him in his work Nitrous oxide combined with a basal of an ultra short-acting barbiturate followed by ethylene or nitrous oxide intratracheally may be used However, the spasmogenic effect of the barbiturates is frequently a source of annoyance during surgery It also may cause respiratory depression and contribute to an already existing anoxia or respiratory acidosis Some induce respiratory paralysis with curare and maintain respiration artificially

Ether is not as desirable as cyclopropane because such operations are usually long and the patient ultimately is saturated with the drug The elimination of the ether is slow and patients may be narcotized for con-

pleural cutaneous fistula is present on occasions. Often an associated pneumonitis is present.

Relaxation is not a factor in drainage of the space or other operations on the pleura. The patient is usually placed in the upright sitting position for thoracotomy to facilitate drainage. Regional anesthesia, usually paravertebral block, is used. The patient is conscious. He is easily placed and remains in the upright position. Intercostal block is not as satisfactory as paravertebral block for this purpose. When general anesthesia is required cyclopropane intratracheally is the most suitable choice because it is nonirritating, allows adequate oxygenation, is characterized by a rapid induction and is followed by rapid recovery. When cyclopropane is contraindicated ether preceded by ethylene or nitrous oxide may be used. Nitrous oxide combined with a basal or an ultra short acting barbiturate may be used but is not desired because of the spasmogenic nature of the barbiturates and the depression of respiration which follows in the postoperative period.

Drainage of an empyema by use of trocar or injection of air into the pleural space is performed with local anesthesia.

## Lung

A pneumonectomy may be either partial or complete. A partial pneumonectomy, or lobectomy, as it is called, is more tedious and time consuming than a complete one because the individual vessels, bronchi and other hilar structures must be dissected and identified. Partial pneumonectomy is performed for suppurative diseases, removal of foreign bodies, benign tumors or tuberculosis. Occasionally a portion of a lung is removed because an existing foreign body cannot be dislodged or removed by bronchoscopy or other techniques. Complete pneumonectomy is performed for removal of malignant tumors. Pneumonectomy is technically less difficult and meticulous than lobectomy.

Patients undergoing pneumonectomy have diminished pulmonary reserve more often than not. When the operation is performed for suppurative diseases sepsis and all its manifestations are usually present. Sepsis may also complicate neoplastic diseases if the tumor mass is large and long standing. Atelectasis is not an uncommon complication. If mediastinal nodes are enlarged due to infection or metastasis paralysis of the vocal cord may be present particularly on the left side. Inasmuch as the chest is open and pneumothorax is present, assisted or controlled respiration is invariably necessary to maintain proper ventilation. Relaxation is not a requisite. Many pneumonectomies and almost all lobectomies are performed with the patient in the lateral position. Some pneumonectomies may be performed in the supine position. This position, of course, simplifies anesthesia and permits adequate ventilation.

Some surgeons prefer the prone position for resection of a lobe for tuber-

depending on the size and fixation of the gland Thymectomy is usually performed in the supine position The possibility of massive hemorrhage due to technical error or from the trauma to the great vessels, is ever present Bilateral pneumothorax may occur Controlled or assisted breathing is required Therefore, an endotracheal tube is mandatory Reflexes of various types arising from stimulation of the costal and intrathoracic structures are encountered frequently Bronchial spasm may result from these reflex stimulations Changes in pulse rate and variation in blood pressure may also be manifestations of reflex stimulation As in the case of pneumonectomy, cyclopropane intratracheally is the anesthetic of choice When cyclopropane as the sole agent is contraindicated or not desired, ether combined with cyclopropane may serve the purpose admirably Ether preceded by nitrous oxide or ethylene may likewise be used but is less desirable than cyclopropane ether mixtures If a cautery is used a basal of nitrous oxide with thiopental supplies a non flammable anesthetic Of course the objectionable features to thiopental are the same as those when used for pneumonectomy,—that it causes bronchial spasm and a respiratory depression in the postoperative period Local anesthesia is not satisfactory for this type of surgery as it does not provide adequate pain relief Besides patients experience considerable discomfort and are not able to be cooperative

Removal of dermoid cysts, benign and malignant neoplasms, and performance of biopsies are managed in the same manner from the anesthetic standpoint as thymectomy

Anesthesia for operations on the aorta and other great vessels in the mediastinum is managed in the same manner as that for pneumonectomy and mediastinal operations These are confined to *grafting of the aorta* and other vessels for excision of aneurysms, correction of arteriovenous fistulae, and resections for coarctation

## HEART

Operations upon the heart, rarities a decade ago, are common in present day surgical practice These may be subdivided into operations on the pericardium and operations on the heart proper The most common operations upon the pericardium are incision for drainage of collections of fluid, purulent material or blood, and lysis and removal of a thickened, adherent pericardium

Operations upon the heart proper involve suturing of lacerations resulting from trauma, removal of foreign bodies, correction of intra and extra cardiac-congenital defects and the correction of valvular defects due to disease Operations designed to encourage the development of collateral circulation between the blood supply of the chest wall or the omentum and the vessels of the pericardium in cases of coronary artery disease are also attempted

siderable time after the conclusion of surgery The combination of nitrous oxide intratracheally, thiopental and a muscle relaxant is used by certain anesthetists but has well defined drawbacks Complete curarization is induced and ventilation is maintained by controlled respiration The practicability and safety in using this technique is a matter of dispute Discrete anesthetists do not employ it Wherever possible the use of non volatile central nervous system depressants is not advised for thoracic surgery because of the untoward responses on the respiratory system postoperatively Local anesthesia or regional blocks are not satisfactory for pneumonectomy or any exploratory thoracotomy

Anesthesia for *exploratory thoracotomy* in contemplation of a pneumonectomy is managed in exactly the same manner as that for a pneumonectomy

Anesthesia for *incision and drainage of a lung abscess* is managed in the same manner as anesthesia for pneumonectomy Some surgeons attempt to perform the operation with local anesthesia Local anesthesia is not always satisfactory particularly if the exudate in the tracheobronchial tree is excessive Coughing and retching impede the surgeon's progress Ultimately general anesthesia is requested after the operation has been in progress some time It is then more difficult to induce it Asphyxia from sudden flooding of the tracheobronchial tree with purulent exudate is not an uncommon occurrence even when local anesthesia is used As a matter of fact endotracheal anesthesia is safer in this regard because the secretions may be readily suctioned through the catheter Local anesthesia does not permit this

## Mediastinum

Mediastinal operations, as a rule, are managed in the same manner as other intra thoracic operations In the upper mediastinum thymectomy, excision of neoplasms such as dermoid cysts, and operations on the great vessels are the most common procedures encountered Of course operations on the heart are mediastinal operations also However these are dealt with under a separate heading

### Thymectomy

Thymectomy is frequently associated with myesthenia gravis in adults Pressure upon the trachea may be present but it is usually not sufficient to cause obstruction in most instances Symptoms of pressure due to obstruction of the airway by compression may be present in infants and children who have an enlarged thymus The requirements for anesthesia from the surgeon's standpoint differ little from those for other intrathoracic operations and pneumonectomy No relaxation is required Ribs must be resected or the sternum split The operations are usually tedious and long

are those of Potts and Blalock. In the former a shunt is created between the pulmonary artery and the aorta. In the latter one is created between the pulmonary artery and the subclavian arteries. The management of anesthesia for these requires little or no relaxation. As high an oxygen tension as possible is used. A rib resection is mandatory for proper exposure.

In general the requirements and management of anesthesia are the same as for other mediastinal explorations. The method of choice appears to be ether intratracheally, induced with cyclopropane, nitrous oxide or ethylene. A basal of thiopental or other barbiturate intravenously or rectally reduces excitement and apprehension. This is highly desirable because any exertion causes increased cardiac output and marked decreases in blood oxygen saturation. Cyclopropane intratracheally without ether is used by a minority who do not fear the cardiac effects of the drug. Nitrous oxide combined with a basal of thiopental may be used but is also less desirable because non volatile drugs cause respiratory depression during operation and in the postoperative period. Besides, a high oxygen tension cannot be maintained. Sedation, particularly with narcotics should be used sparingly if at all because these patients appear sensitive to these drugs and readily develop respiratory depression. Secretions should be minimized with anticholinergic drugs.

## Closure of Patent Ductus Arteriosus

Anesthesia for closure of a *patent ductus* arteriosus is managed in the same manner as that for correction of congenital defects by the Blalock or Potts operation. In these subjects cyanosis is not a problem. The diastolic pressure is lowered, the systolic is elevated. The diastolic pressure often rises after the ductus is ligated. In infants and young children cardiac function is not impaired. As a matter of fact the myocardium in infants and children appears to withstand the usual surgical trauma imposed during correction of congenital defects quite well. It is in older children and young adults that function is impaired. The adult who has a patent ductus arteriosus frequently shows some cardiac enlargement. Heart failure supervenes much more readily in adults than in children. The operation for closure of a ductus is performed with the patient in the supine position. An open chest necessitates the use of an endotracheal airway and controlled respiration as in the case of correction of lesions caused by disease and trauma which are being treated surgically.

## Other Cardiac Operations

Anesthesia for *suturing of the myocardium* from penetrating wounds of the heart or removal of foreign bodies is managed in the same general manner as that for explorations of the mediastinum. Endotracheal ether preceded by cyclopropane, ethylene or nitrous oxide is used. The combination

## Operations on the Pericardium

Lysis of adhesions or removal of adherent thickened pericardial tissue is usually performed for tuberculosis, constrictive pericarditis, or polyserositis (Pick's Disease) Irritability of the myocardium may be present Polyserositis is frequently accompanied by an enlarged liver and ascites The patients are usually children or young adults Surgical exposure for a pericardiotomy necessitates resection or splitting of the sternum Local anesthesia is used for *incision and drainage* in acutely ill subjects *Resections* and *suturing* of the pericardium require general anesthesia Non traumatic inductions are essential for pericardial surgery A basal of thiopental fol lowed by ethylene, nitrous oxide or cyclopropane with an ether sequence is the usual choice A muscle relaxant is used to facilitate intubation The combination of nitrous oxide and thiopental is a less desirable choice al though it is used by some

## Correction of Congenital Anomalies

Operations for correction of congenital anomalies of the heart are being performed with increasing frequency It would be out of the question to attempt to discuss at this time all the possible defects encountered The most common anomaly for which correction is attempted is the Tetralogy of Fallot In general most anomalies do one or a combination of three things (1) prevent sufficient blood from passing through the lung, (2) allow venous and arterial blood to mix, or (3) they compress or obstruct vital structures such as the trachea, bronchi, esophagus or vagus nerves The operations for these conditions therefore are directed towards creating shunts to permit more blood to flow through the lung, closing defects to prevent mixing of arterial and venous blood or reconstructions to overcome interference of activity of extracardiac structures

*In all cardiac surgery it is most desirable to use methods of anesthesia* which do not decrease cardiac output Any factor which causes an increase in oxygen consumption is to be scrupulously avoided *Hypothermia* is deliberately induced by some surgeons by cooling the subject on special mattresses through which ice water circulates This is done to reduce the metabolic rate which in turn lightens the cardio respiratory load

## Tetralogy of Fallot

Most patients undergoing surgery for the Tetralogy of Fallot are infants or children Adults, however, are occasionally seen also The patients all have a hematocrit which is above normal, an increased blood viscosity and an expanded blood volume The arterial blood oxygen saturation is below normal Symptoms of impediment of blood flow through the lungs are always present The operations most frequently performed for this entity

instrumentation or from foreign bodies, to excise diverticuli and to resect for malignant tumors When the disease for which the operation is performed has been long standing and has been of such a nature that nutrition has been impaired manifestations of weakness, anemia and cachexia are invariably present If the patient's condition is poor, a gastrostomy may be advisable to restore the blood volume and general physical state to normal before the exploration and a resection is undertaken Operations upon the esophagus are invariably long and tedious As in the case of other thoracic operations an open chest is required Esophageal operations are most often performed with the patient in the lateral prone position although some may necessitate the supine position which, of course, is preferable Usually a stomach tube is introduced prior to anesthesia This often interferes with the proper fitting of the mask and makes induction and maintenance of anesthesia difficult An endotracheal tube must be used to secure a tight "fit" When diverticuli are present in which retention of food and fluid can occur aspiration from regurgitation is an additional hazard Reflex changes of the vagal type due to manipulations of the esophagus are common Cardiac arrest ascribed to vago vagal reflexes from manipulating the lower esophagus is a possibility However the incidence of cardiac arrest from this cause is uncommon

Cyclopropane intratracheally is satisfactory for esophagectomy If arrhythmias occur and cyclopropane cannot be used alone, ether is added Nitrous oxide and a basal of thiopental with controlled respiration, is used by some anesthetists If the operation is long respiratory depression may follow in the postoperative period due to the cumulative effects of thiopental Local or regional anesthesia is not suitable unless the operation is upon the cervical portion of the esophagus Local anesthesia cannot be used for resections of the upper thoracic portion

## Diverticulectomy of the Esophagus

Diverticuli may occur anywhere in the esophagus When located in the cervical portion local anesthesia may, on occasions, be used Some surgeons prefer local anesthesia because the patient is able to "blow" to inflate the diverticulum to facilitate its identification for resection When the use of local anesthesia is not feasible the technique and conduct of anesthesia is similar to that ordinarily used for esophagectomy

## Other Esophageal Operations

Anesthesia for incision and drainage of *periesophageal abscesses* due to perforation from trauma of a neoplasm, or those resulting from suppuration of nodes is managed in the same manner as anesthesia for esophagectomy *Resections*, reconstrictions, *repairs of tears* and perforations are managed in the same manner

of nitrous oxide and a basal of thiopental and a muscle relaxant may be used to facilitate induction

### Valvulotomy

Valvulotomy is usually performed when a stenosis exists due to scarring from rheumatic fever or arteriosclerosis The valve most frequently in volved is the mitral valve Operations for release of stenosis of the aortic valve are performed less frequently The majority of these patients have had previous rheumatic fever Auricular fibrillation, cardiac failure and undiagnosed active rheumatic fever may be present Cardiac failure or auricular fibrillation sometimes develops when the operation has been in progress some time The possible occurrence of pulmonary edema during operation must be borne in mind Hemoptysis may occur during anesthesia when severe mitral stenosis is present As with other cardiac operations these are performed in the supine or semi lateral position as a rule Ether intratracheally preceded by an induction with cyclopropane, nitrous oxide or ethylene is satisfactory for valvulotomy A basal of thiopental intra venously or rectally may be used to reduce apprehension Some anesthetists fear cyclopropane and exclusively use nitrous oxide or ethylene for induc tion A basal of thiopental followed by nitrous oxide intratracheally com bined with thiopental may be used but is not as satisfactory as cyclopropane ether because the non volatile drug, particularly when given to excess, causes respiratory depression in the postoperative period Local anesthesia is not satisfactory for this type of surgery because of its formidable nature, dura tion and the discomfort experienced during the procedure The technique and anesthetic management is basically the same for other mediastinal operations

In all cardiac surgery it is customary to continuously record the electro cardiographic pattern throughout operation The anesthetists and other members of the operating team should be prepared to cope with cardiac arrest A defibrillator and various cardiac stimulants and depressants are kept on hand Procaine amide, quinidine or intravenous procaine are used to depress the heart and reduce irritability and calcium chloride, digitalis and epinephrine to stimulate it in the event of emergency In the cases where the blood volume is above normal the operating team must be pre pared to do a phlebotomy should the indication arise Fluid administration is closely watched and correlated with blood volume and hematocrit studies

## ESOPHAGUS

Operations on the esophagus, unusual a decade ago, are commonplace today They are performed for a variety of conditions Areas due to stric- tures and chemical burns, most often lye, are resected and *reconstructed* They are also performed to remove fibrotic growths, to suture tears due to

BURSTEIN C L ALEXANDER F D A Anesthesia for thoracic surgery *Anesthesiology, 8* 36–50 1947
BJORK V O CARLENS E FRIBERGO O Endobronchial anesthesia *Anesthesiology 14* 60–72 1953
GRUENWALD C SWORD B Thoracic operations for pulmonary tuberculosis *Anesthesiology 10* 295–318 1949
GUILD C H Anesthesia for thoracic surgery *Anesthesiology 12* 733 1951
HARRIS A J Management of anesthesia for congenital heart operations *Anesthesiology 11* 328–332 1950
HARMEL, M H LAMONT A Anesthesia in the treatment of congenital pulmonic stenosis *Anesthesiology 7* 477–487 1946
NEFF W PHILLIPS GUNN G Anesthesia for pneumonectomy in man *Anesthesiology 3* 314–322 1942
PENDER J W Anesthesia for mitral commissuotomy *Anesthesiology 14* 77–84 1953
SMITH R M Factors in anesthesia in surgery for congenital heart disease *Anesthesiology 13* 38–50 1952
SOMMERFIELD R B Anesthetists interest in lipoids bronchography *Anesthesiology 3* 61–64 1942
WILHEM A R Anesthesia for oesophageal surgery *Anesthesiology 3* 274–279 1943

### Tracheoesophageal Fistulae

Patients with tracheoesophageal fistulae are usually newborn Sometimes the diagnosis is made at or shortly after delivery, in which event the operation is performed immediately The sooner it is performed the less the possibility of pneumonitis As a rule though, the anomaly is not recognized immediately and gastric contents and swallowed material spill into the lung and cause pneumonitis Also, other congenital anomalies may co exist with this one To close the fistula an intrathoracic approach is required The operation is tedious and time consuming Ether-oxygen is the usual choice Endotracheal catheterization is necessary because positive pressure, controlled breathing, frequent aspiration of secretions are necessary The ether may be insufflated by the Ayre technique or given with oxygen by the semi-closed, non rebreathing method There is no objection to the closed system if the apparatus is adequate Cyclopropane may be used if the closed system is available Non volatile drugs such as thiopental are undesirable particularly if pneumonitis exists

## THE DIAPHRAGM

Diaphragmatic operations consist of repairs of hernias, suturing of rents due to rupture from trauma or reconstructions of congenital anomalies Hernias are acquired or exist congenitally Patients with afflictions of the diaphragm may manifest disturbances of respiration This may be true particularly when there has been eventration and the abdominal contents are in the thoracic cage Gastric re ention may be present If so, a stomach tube should be used for decompression prior to induction of anesthesia to avert regurgitation and aspiration The trans abdominal approach is used more often than the thoracic for these operations It is advisable to be prepared to deal with an open chest and to have an endotracheal catheter in place at all times The surgeon may encounter technical difficulties and be compelled to open the chest even though he begins the operation through a trans abdominal incision Accidental perforation of the diaphragm may be a technical complication The anesthetist must be prepared to institute controlled respiration and positive pressure to cope with the pneumothorax which invariably follows Cyclopropane, cyclopropane ether mixtures or nitrous oxide or ethylene ether sequence are the usual choices for this type of surgery Nitrous oxide combined with a basal of thiopental and a muscle relaxant may be used but presents the usual objections of possible respiratory depression and troublesome traction reflexes

### REFERENCES

ADELMAN M H Anesthesia in surgery of patent ductus arteriosus *Anesthesiology* 9 42–47 1948

ALEXANDER F D A *et al* Anesthesia for thoracoplasty *Anesthesiology* 9 637–643 1948

CLINICAL RECORD | ANESTHESIA

CHOLECYSTECTOMY

☐ GOOD ☐ FAIR ☐ POOR

PREMEDICATION

INDUCTION

MAINTENANCE

ENDOTRACHEAL

RECOVERY

ABDOMEN OPEN

TRACTION

GALLBLADDER OUT

CLOSURE

180

160

140

120

100

80

60

40

20

10-2614g-2

ANESTHESIA

FIG 33 The changes in blood pressure caused by the celiac plexus reflex A lowering in systolic pressure a fairly well maintained diastolic pressure a narrowed pulse pressure and a bradycardia characterize this hypotensive state This hypotensive state, obviously of neurogenic origin is frequently relieved by anti cholinergic or sympathomimetic drugs

## XXXII

# INTRA-ABDOMINAL OPERATIONS

The most important requisite for anesthesia for all types of abdominal surgery is muscle relaxation Without relaxation the surgeon may be handicapped and cannot operate easily and deftly The abdominal muscles particularly the recti, are more powerful than is realized Lower second or upper third plane anesthesia is necessary to obtain satisfactory relaxation most of the time At times even deeper anesthesia is required

Anesthesia for upper abdominal surgery is more difficult to manage than that for lower abdominal and pelvic surgery because the upper recti are larger, better developed and more difficult to relax In the upper abdomen the viscera move up and down with each diaphragmatic excursion and interfere with surgical manipulations As a rule procedures in the upper abdomen are lengthy, tedious and usually of a serious nature Traction on the mesenteries and viscera initiate reflex activity which cause respiratory and circulatory disturbances Two reflexes, the celiac axis reflex and the Brewer Luckhardt reflex are encountered is most abdominal surgery, but particularly that of the upper abdomen The celiac plexus reflex is characterized by lowering of both systolic and diastolic pressures narrowing the pulse pressure and bradycardia (Fig 33) The Brewer-Luckhardt reflex causes both circulatory changes and reflex laryngeal spasm The laryngeal spasm interferes with adequate minute volume exchange and prevents free respiratory movements The conduct of inhalation anesthesia is difficult under these circumstances and surgical manipulations are not simplified by any means

In the lower abdomen these reflexes, if they are present, are nowhere near as troublesome Likewise in the lower abdomen the impulses of the diaphragmatic excursions are transmitted with decreased magnitude The recti and other muscles of the abdominal wall are not as well developed and therefore easier to relax When the peritoneal cavity is entered during a surgical operation and the peritoneum is stimulated, particularly when anesthesia is light, the abdominal muscles reflexly become tense If an incision is made under such circumstances the abdominal viscera will be forced outward When spinal anesthesia is used for abdominal surgery sensory anesthesia must extend to the xyphoid, otherwise, the patient experiences discomfort when the parietal peritoneum and viscera are manipulated Retching, nausea and vomiting occur because the autonomic reflexes continue to be transmitted along the vagi and also in a retrograde manner along the sympathetic chains into the cord above the level of blockade

manipulations also initiate nausea and vomiting which hamper the surgeon considerably. The incidence of postoperative respiratory complications in upper abdominal surgery performed with spinal anesthesia is approximately twice that done with general anesthesia. Atelectasis and pneumonitis occur more frequently after spinal anesthesia has been used. Field block or intercostal block combined with ethylene, light cyclopropane and nitrous oxide anesthesia is often used for surgery for poor risk subjects. When field blocks are used better results are obtained if they are supplemented with a splanchnic block in order to obtund the visceral reflexes which give rise to the discomfort caused by manipulating the intra abdominal structures. When employed by skillful, gentle surgeons such a choice may be justified, but in the hands of unskilled operators less trauma is apt to be inflicted if general anesthesia is used instead. Poor risk subjects, often operated upon with this type of anesthesia, would do better if general anesthesia were used.

*Cholecystotomy* is usually performed on patients who are too ill to withstand cholecystectomy. The problems differ little from those for cholecystectomy. Some surgeons prefer local anesthesia for these operations. This may be justified when the patient is extremely ill, but otherwise general anesthesia is used. The choice and conduct is similar to that for cholecystitis.

## The Bile Ducts

Exploration of the bile ducts or choledochostomies may be time consuming. They are usually performed on patients who have been ill for some time. Many have, or have had jaundice. Some come to surgery for reoperation because previous biliary tract surgery was unsatisfactory. Scaring, stenosis, fistulae or other complications of previous operation may require re exploration or additional surgery. The management of anesthesia for these patients differs in no way from that for cholecystectomy. *Cholecystogastrostomy* or *cholecystenterostomy* are performed for obstructive jaundice particularly if caused by carcinoma of the head of the pancreas or other intrinsic and extrinsic factors blocking the duct. These patients are chronically ill. More often than not, they have jaundice, and are emaciated. They do not withstand formidable surgery. Light anesthesia using cyclopropane intratracheally is preferred. Field block or intercostal block combined with nitrous oxide, ethylene or light cyclopropane anesthesia may be used. Non volatile drugs, such as thiopental, large doses of morphine, muscle relaxants are used sparingly or best not used for patients with jaundice particularly when the jaundice has been long standing.

The choice of anesthesia for *resections for carcinoma of the biliary* tract is managed in the same manner as that for common duct exploration.

## Stomach

Operations on the stomach consist of resections complete or partial, gastro enterostomies, vagotomies or gastrostomies. The physical condition of

Discomfort is frequent when local infiltration, intercostal, or abdominal field block are used for surgery unless the splanchnic nerves are blocked

## Surgery of the Biliary Tract

Operations on the biliary tract usually involve the gall bladder, the bile ducts and the duodenum *Cholecystectomy* is the simpler of the operations performed upon the biliary tract Patients undergoing cholecystectomy are *usually middle aged, obese, short in stature with a short neck and a thick abdominal wall Hypertension or diabetes or other degenerative diseases are* often complications In acute cholecystitis fever, leukocytosis, dehydration and other signs of infections are present The abdomen is usually rigid In biliary tract surgery the surgeon frequently has difficulty in securing adequate exposure, therefore, as much relaxation as possible must be provided The duration of operations upon the biliary tract depends largely on the conditions encountered and the skill and dexterity of the surgeon Usually such operations last an average of 1½ to 2 hours Structures cannot be readily identified when adhesions are numerous This adds to the operating time in certain cases Cholecystograms may be taken during the operation for confirmatory purposes This necessitates the use of X ray apparatus and a fire hazard is thereby created Traction on the mesenteries and structures of the biliary tract initiate reflexes which cause laryngeal spasm and circulatory changes The Brewer Luckhardt reflex occurs more frequently during biliary tract manipulations than when other upper abdominal procedures are being performed The so called "celiac plexus reflex" also occurs frequently, particularly during ether anesthesia

For patients considered to be good risks cyclopropane intratracheally combined with a muscle relaxant is satisfactory A basal of thiopental may be used prior to induction of anesthesia Ether may be added if one chooses Should cyclopropane be contraindicated ether intratracheally preceded by nitrous oxide or ethylene may be used A muscle relaxant, depending upon whether or not relaxation is obtained with ease, may also be used Nitrous oxide combined with a basal narcosis of thiopental and a muscle relaxant may be used but is a less desirable choice An endotracheal catheter is highly desirable for upper abdominal surgery Besides assuring a patent airway it also prevents jerky spasmodic respiration due to traction upon the gall bladder and other structures Also controlled respiration may be used

Spinal anesthesia is demanded by many surgeons for biliary and other upper abdominal surgery because it affords excellent relaxation However, it is not as satisfactory as it appears at first glance As a rule, all is well until traction is made upon the gall bladder Pain impulses then pass in a retrograde manner along the sympathetic ganglia and into the cord above the area of blockade The patient experiences pain in the shoulder, the neck or in the chest particularly around the heart This discomfort is difficult to obliterate unless the spinal anesthetic is supplemented with a general anesthetic The

gastrectomy The same principles and contraindications apply

*Esophagastrectomy* is usually performed for neoplastic diseases, varices, or ulcerative lesions The transthoracic approach is used by some surgeons Others use the abdominal approach and follow it with the thoracic or vice versa Endotracheal cyclopropane or cyclopropane ether is the best choice for this type operation If cyclopropane is contraindicated ether intratracheally preceded by nitrous oxide may be used Muscle relaxants may be used to secure adequate relaxation Nitrous oxide combined with a basal of thiopental and a muscle relaxant is used by many but is a less desirable choice An endotracheal catheter is required when this combination is selected Spinal anesthesia is not satisfactory for this type of surgery Positive pressure and assisted or controlled respiration may be necessary because of the open chest

Patients who have *perforated gastric* or duodenal ulcers are, without exception, acutely ill Often they are in shock, sometimes they are dehydrated The abdomen is rigid and board like The operation in the hands of an expert surgeon is quickly performed but requires an extreme degree of relaxation to overcome the board like rigidity Most surgeons prefer spinal anesthesia However, spinal anesthesia is contraindicated if the patient is or has been in shock Ether or cyclopropane intratracheally combined with a muscle relaxant is preferable under these circumstances Nitrous oxide with a basal of thiopental is not a desirable choice unless the patient is in poor condition Field or intercostal block may be used when the patient is in extremely poor condition but as a rule they are not as satisfactory as other forms of anesthesia

## The Pancreas

Explorations in which acute pancreatitis is encountered are usually the results of errors in diagnosis Few surgeons who are aware of the diagnosis will operate upon patients so affected These patients are acutely ill, usually have a board like rigidity, fever, leukocytosis and marked abdominal distention Hypotension and a shock like state may be present or frequently supervene after anesthesia has been induced For this reason it is best to avoid spinal anesthesia when this disease is suspected Ether or cyclopropane intratracheally with or without a muscle relaxant is by far the best choice

### Resections of the Pancreas

Operations most commonly performed on the pancreas are resections for carcinoma or removal of cysts Resections are usually long procedures Many patients with pancreatic disease are chronically ill, show signs of anemia, emaciation and cachexia as a result of digestive disturbances Some have jaundice Anesthesia for pancreatic surgery is managed in the same manner as that for biliary surgery and other upper abdominal operations, bearing in mind, of course, that they are long and time consuming Effects of

patients undergoing gastric surgery varies considerably Chronically ill subjects whose nutrition has been poor may have anemia, low serum proteins, vitamin deficiencies, electrolyte imbalance, weight loss and so on

## GASTRECTOMY

Gastrectomies are usually performed for gastric or duodenal ulcers, neoplasms and for uncontrollable gastric hemorrhage The patients are middle aged or old rather than young Preoperative preparation with blood, proteins, electrolytes and so on is important as in the case of biliary tract surgery Traction reflexes are almost as great a problem as in biliary surgery Retention may be present particularly if there is a neoplasm or scarring at the pylorus A stomach tube is usually necessary preoperatively and during anesthesia for decompression It is advisable to withdraw the tube before anesthesia is induced after the stomach is evacuated to simplify maintenance of anesthesia technically and to reduce possibility of aspiration

Patients who are operated upon for gastrectomy for gastric hemorrhage usually have been in shock or are in shock The selection of anesthesia differs little from that for other gastric surgery if the blood pressure is stabilized Cyclopropane intratracheally or ether intratracheally with a muscle relaxant is a satisfactory choice Light cyclopropane anesthesia combined with field blocks may be used to perform the surgery in poor risk exsanguinated patients The use of spinal or deep ether anesthesia or muscle relaxants and thiopental is not advised where bleeding is a factor Local anesthesia may be used for extremely poor risk cases

*Gastrostomy* is usually performed when an obstruction exists at the pylorus Patients necessitating such surgery may be dehydrated, emaciated, have avitaminosis and other nutritional deficiencies if the disturbance has been long standing When the obstruction is acute and the physical status is good, anesthesia is managed in the same manner as that for other operations in the upper abdomen Aspiration from regurgitation of retained stomach contents is always a possibility when lesions causing obstruction are present In the emaciated sickly poor risk patient local anesthesia is usually preferred

Anesthesia for *gastro enterostomy* is managed in the same manner as that for other gastric operations Usually obstruction is present when this procedure is indicated Aspiration must be guarded against The patient is, as a rule, emaciated, dehydrated, has nutritional deficiencies and is a poor risk Field block or intercostal block combined with nitrous oxide or light cyclopropane anesthesia may be used Light cyclopropane anesthesia with infiltration of the rectus muscle is also preferred by some surgeons This combination works admirably Muscle relaxants are best avoided in poor risk subjects undergoing upper abdominal surgery When the condition of the patient is good the choice is similar to that outlined for gastrectomy

*Vagotomy* may be performed with the type of anesthesia recommended for

without an endotracheal tube is used by many but an endotracheal tube is preferred as it provides an adequate airway and obviates the laryngeal spasm or reflex origin

## RETROPERITONEAL EXPLORATIONS

Retroperitoneal explorations are usually performed for removal of neoplasms, biopsies, repair of hernias, control of bleeding, evacuation of hematomas and abscesses and so on

The removal of retroperitoneal masses when the trans abdominal approach is used in the upper abdomen requires the same type of anesthesia recommended for pancreatic and gastric and other upper abdominal surgery The removal of masses in the lower abdomen also is the same Also the repair of *internal hernias* likewise requires a similar type of anesthesia When the extra peritoneal approach is used through a lateral or posterior incision the technique is as described for nephrectomy and sympathectomy

### Intestines

#### Resections

Anesthesia for intestinal surgery whether on the large or small bowel is managed essentially in the same manner as that for gastric and biliary surgery Most intestinal resections, enterostomies, and enterotomies may be performed adequately with spinal anesthesia, cyclopropane or ether intratracheally provided the subject is a good risk A muscle relaxant may be necessary but is not used routinely The combination of nitrous oxide and thiopental with a muscle relaxant may also be used although it is a less desirable choice In poor risk subjects, an intercostal or abdominal field block combined with light cyclopropane, ethylene or nitrous oxide anesthesia may be used Local anesthesia is reserved for extremely poor risk subjects Ether is undoubtedly the best choice for intestinal surgery on infants and children The open drop method is satisfactory if the closed or semi-closed apparatus is not available

#### Intestinal Obstruction

Laparotomy for relief of acute intestinal obstruction presents difficulties for both the anesthetist and the surgeon particularly when the condition is in the advanced stages The patients are acutely ill, distended, and dehydrated There may be disturbances of blood electrolytes, acid base balance, and renal function Fecal vomiting and shock may also be present Unless the obstruction is recognized and treated early such patients usually do poorly during and after surgery The surgeon is hampered by the distended and dilated loops of bowel The anesthetist is confronted with the problem of regurgitation and aspiration and providing extreme degrees of relaxation Drowning from aspiration of vomitus is not an uncommon occurrence during

reflexes, difficulty in obtaining relaxation and other technical problems of anesthesia for gastrectomy or biliary tract surgery are also encountered in this type of surgery

## Spleen

### *Splenectomy*

Operations involving the spleen are performed for removal of the organ Splenectomy is usually performed for traumatic rupture, for relief of blood dyscrasias or when there is marked enlargement with fibrosis as is encountered in certain of the splenomegalies The chief concern when rupture is present or suspected is shock from hemorrhage Drugs and techniques of anesthesia which may be complicated by anoxia or hypotension are avoided Spinal anesthesia since it induces hypotension should not be used under these circumstances Cyclopropane intratracheally combined with a muscle relaxant or ether intratracheally are the best choices under these circumstances Splenectomy performed for blood dyscrasias may be complicated by anemia, jaundice and a tendency toward bleeding due to disturbances in the clotting mechanism or deficiency of platelets The bleeding tendency is of concern to both the anesthetist and the surgeon The anesthetist carefully avoids instrumentation with airways, laryngoscopes, needles and catheters, etc for fear of initiating incontrollable hemorrhage

Some surgeons inject epinephrine into the splenic artery to cause the spleen to contract in order to force the blood contained by the organ into the arterial system before the pedicle is clamped This must be borne in mind if the use of cyclopropane is contemplated Epinephrine is contraindicated Ether causes the normal spleen to constrict Cyclopropane does not Spinal anesthesia causes the normal spleen to dilate

Anesthesia for splenectomy for cirrhosis or Banti's disease is managed in the same manner as that for splenectomy for other diseases A fibrotic spleen does not contract under nervous or hormonal influence The use of drugs which do, to secure contraction of such a spleen is met with disappointment Some surgeons prefer spinal anesthesia for splenectomy It may be used if anemia or shock are not complicating factors Cyclopropane or ether intratracheally combined with a muscle relaxant is the better choice A less desirable choice, even though many use it, is nitrous oxide combined with a basal of thiopental and a muscle relaxant The cumulative action and respiratory depression are objectionable features Hemorrhage, traction reflexes, and oozing from adhesions are some of the technical difficulties encountered in attempting to remove the spleen The surgeon frequently explores further in search of accessory spleens which may lengthen the time during which profound anesthesia is required

The majority of subjects undergoing splenectomy are children The management of anesthesia in these subjects is similar to that in adults Ether

sired cyclopropane with a muscle relaxant or cyclopropane ether are satisfactory Thiopental, nitrous oxide and a muscle relaxant are used by many but are less desirable because of the large amount of barbiturates used over the long period of time

### Intra Abdominal Suppuration

Intra abdominal abscesses may occur anywhere but are usually located in the pelvis or in the subhepatic or subdiaphragmatic areas Infections of the genito urinary tract give rise to abscesses in the upper quadrants, appendicitis in the caecal area, and perforation of diverticulae in the sigmoid area Perforations of the stomach or gall bladder and rupture of abscesses in the liver from amebic and pyogenic infection give rise to abscesses in the subdiaphragmatic area on either the left or right side Abscesses may follow infections anywhere in the peritoneal cavity, however Patients who have intra abdominal abscesses are usually acutely ill Signs of sepsis, fever, and leukocytosis are present and such patients are often referred to as "toxic" Dehydration, electrolyte disturbances, acidosis due to vomiting and inability to eat are present When acutely ill these patients do not withstand any formidable surgery or extensive manipulations Usually they are operated upon for exploration, or incision and draining of the abscess Cyclopropane is usually an excellent choice of anesthesia for these subjects because it disturbs metabolic processes little if at all Besides it is labile and affords adequate relaxation most of the time Ether may be used if cyclopropane is contraindicated Muscle relaxants may be used cautiously The combination of thiopental, nitrous oxide and a muscle relaxant is a less desirable choice and contraindicated when the patients are severely ill Marked depression of respiration and slow recovery in the postoperative period seems to be common in these patients when these drugs are used The use of spinal anesthesia is advised only when the abscesses are in the lower abdomen in the patient who is in fairly good condition Field block and local infiltration may be used in poor risk subjects or in those in whom the abscess is superficial, well localized and easily accessible

## LOWER ABDOMINAL SURGERY

Anesthesia for lower abdominal surgery does not differ remarkably from that for upper abdominal surgery Although relaxation of approximately the same degree is required it is obtained with greater ease Obviously this type of abdominal operation varies in duration depending upon the procedure performed Appendectomy, and operation on the pelvic organs as a rule in the hands of skillful operators usually require 1 to 2 hours Resections of the bowel in the lower abdomen like those in the upper may occupy considerably more time The requirements for surgery, status of patient and anesthetic problems differ little from resections in the upper abdomen

explorations for intestinal obstruction if patients are poorly prepared preoperatively As much of the stomach contents and intestinal gas as possible should be aspirated before the patient is brought to surgery

When the obstruction has persisted for some time, and this is often the case, a rapid induction using cyclopropane or a thiobarbiturate intravenously is advised A muscle relaxant is administered to facilitate intubation An endotracheal catheter *with a cuff* is quickly introduced A seal is immediately made between the trachea and the endotracheal catheter to avoid aspiration Thus if the patient regurgitates aspiration will be minimized or prevented Ether may be added if the patient is not relaxed or develops an arrhythmia from the cyclopropane Patients with increased intra abdominal pressure from any cause do not tolerate spinal anesthesia A severe uncontrollable hypotension develops which is often difficult to correct with vasopressors Its use therefore is not advised if distention or shock are present Besides regurgitation and aspiration of vomitus cannot be prevented In the recumbent position massive regurgitation is promptly fatal The use of local or spinal anesthesia is no assurance against this since the patient is not able to sit up The cough reflexes are active, it is true, but aspiration occurs regardless Spinal anesthesia may be used for early cases of obstruction The patient is in good condition and there is no distention This method of anesthesia provides excellent exposure and facilitates exploration However cyclopropane or ether intratracheally with a muscle relaxant is equally as satisfactory and preferable

Relief of obstruction is attempted by ileostomy, colostomy or cecostomy when the patient is too ill to undergo exploratory laparotomy *Cecostomy* ileostomy and similar operations are performed with local anesthesia as a rule For patients in good condition spinal or inhalation anesthesia techniques may be used

Colonic resections are performed for removal of new growth, scarred areas due to inflammatory lesions, dilatations, malfunction (megacolon) and so on Elective *colectomies* of the transverse or splenic or hepatic flexures in good risk subjects may be performed with spinal or inhalation anesthesia Cyclopropane ether or cyclopropane alone combined with a muscle relaxant may be used Where a cautery is used and general anesthesia is desired, the combination of nitrous oxide, thiopental and a muscle relaxant is the only choice In poor risk subjects field block or local anesthesia may be used

Combined abdominoperineal resections are with few exceptions long procedures which are usually performed for excision of new growths or scarred areas Most patients are middle aged or in the older age group Shock and blood loss are not uncommon Spinal anesthesia is preferred by most surgeons Nupercaine combined with epinephrine by the single injection method may be used to obtain a prolonged block lasting four or five hours Some use continuous spinal anesthesia If general anesthesia is de-

infants and children There is no contraindication to the use of cyclopropane provided proper apparatus for administering the drug is available and the anesthetist is skilled in the use of the drug in children The use of spinal anesthesia for children is not advised because these subjects are not psychically suited for it Besides it is not induced and maintained as easily and as safely in children as it is in adults The possibility of damaging the cord is greater in children because it extends to a lower vertebral level There is also greater lability of the vascular system

## REFERENCES


ADRIANI JOHN Anesthesia for abdominal surgery Chap in *Pack and Ariel Treatment of Cancer and Allied Diseases* New York Hoeber in Press

FLAGG P J *Art of Anesthesia* 7th Ed Philadelphia Lippincott 1944

GEFFNER B A PERKOWITZ S Prevention of atelectasis or pneumonia following abdominal operations *Anesthesiology* 14 166–179 1953

HALE D E SHAAR C M Splanchnic anesthesia in gastric surgery *Anesthesiology* 5 392–397 1944

NOSWORTHY M D *Theory and Practice of Anesthesia* Brooklyn Chem Pub Co 1940

PALLSO J A Anesthesia for surgical procedures for intestinal obstruction *J Am A Nurse Anesth* 18 250 1950

ROVENSTINE E A Anesthetic control of abdomen *Conn M J* 5 88 91 1941

In selecting anesthesia, the dexterity of the surgeon and his operating time are always considerations The physical status of the patient varies considerably depending upon the surgical disease Some patients are in excellent condition Others may have anemia, jaundice, sepsis and other manifestations of the surgical and other complicating diseases Traction reflexes also are noted during lower abdominal surgery but they are not as prevalent or troublesome, as a rule, as in upper abdominal surgery Nausea, vomiting and regurgitation may occur particularly when dealing with intestinal obstruction, wound disruption, volvulus, peritonitis, or other acute abdominal conditions As in the case of upper abdominal surgery, electrolyte imbalance and other biochemical disturbances may be present particularly if there has been previous interference with nutrition or protracted vomiting or dehydration

Cyclopropane combined with a muscle relaxant is used to a large extent for surgery of the lower abdomen If cyclopropane is not desired ether may be used or may be combined with cyclopropane A muscle relaxant is not necessary as a rule due to the potency of ether A basal of thiopental may be used prior to the inhalation anesthetic The combination of nitrous oxide, thiopental and a muscle relaxant is a commonly used but is a less desirable choice Whether or not an intratracheal catheter is used depends upon the ease of maintenance of the airway In obese subjects its use facilitates anesthesia Spinal anesthesia is ideal for lower abdominal surgery, if the patient is psychically suited for it Frequently patients object to spinal anesthesia because they have heard of an isolated instance of a neurologic complication Others fear being conscious throughout operation In the former case it is best to acquiesce to the patient's wish In the latter the objection may be obviated by using an ultra short acting barbiturate (thiopental) administered by intravenous drip or secobarbital or intravenous morphine and scopolamine after the spinal anesthetic is induced Field block or intercostal block combined with a splanchnic block may be used for poor risk patients Such techniques are satisfactory only in the hands of the most expert anesthetists and operators, however Local anesthesia, as a rule, is not suitable for abdominal surgery It is used in poor risk, moribund patients for cecostomy or ileostomy, incision and drainage of a superficial or an easily accessible abscess

Resuturing for *dehiscence* and *evisceration* are best done with inhalation anesthesia When the patient is in poor condition, and many are, the use of local anesthesia is advised In patients in good condition, cyclopropane combined with a muscle relaxant is suitable Wound disruptions are often complicated by intestinal obstruction Aspiration from regurgitation should be considered a possibility These patients therefore should be examined closely and if evidence of intestinal obstruction exists should be managed in the same manner as those having intestinal obstruction

Ether is the most commonly used anesthetic for abdominal surgery in

## EXTRA PERITONEAL OPERATIONS

Extra peritoneal operations are performed upon the kidneys, adrenal glands, ureters, prostate, and bladder and the autonomic nervous system As is the case in intra peritoneal operations muscle relaxation is necessary to secure adequate exposure

### Kidney and Ureters

#### Nephrectomy

Nephrectomy usually is performed extra peritoneally The operation is performed for sepsis, tuberculosis, removal of stones, malignant disease and so on Renal failure may complicate the surgical disease Abdominal distention of a reflex origin may complicate the picture particularly in cases of colic Patients being operated upon for nephrectomy and other renal operations are usually placed in the lateral prone position unless the operation is performed transabdominally in which case it is done in the supine position Relaxation is required for adequate exposure and easy closure During surgery the adrenal gland is frequently manipulated This may cause circulatory disturbances manifested by tachycardia and hypertension and other signs of sympathetic stimulation

The peritoneum, since it is adjacent to the operative field, is manipulated giving rise to the usual manifestations of such stimulation—namely rigidity of the muscles Troublesome reflexes may occur from traction on the renal pedicle or manipulation of the peritoneum The peritoneal cavity may even be inadvertently entered Nausea and vomiting initiated by traction reflexes occasionally occur when the operation is performed under spinal or local anesthesia Hemorrhage from trauma, slipping of ligatures or loosening of clamps on the renal vessels occurs infrequently but is a possibility which must be borne in mind

The anesthetist often has difficulty maintaining an adequate airway when general anesthesia is used because of the awkward position An endotracheal catheter is desirable The anesthetist must be prepared to administer positive pressure should a pneumothorax develop if the pleural space is inadvertently entered Cyclopropane combined with a muscle relaxant is satisfactory for nephrectomy If cyclopropane is not desired or contraindicated ether may be used preceded by nitrous oxide or ethylene The ether may be combined with a muscle relaxant There is no objection to the use of a basal of thio pental as an induction agent The combination of nitrous oxide, a basal of thiopental and a muscle relaxant may be used but is a less desirable choice Spinal anesthesia is satisfactory from the surgeon's standpoint but less desirable than general anesthesia from the patient's standpoint for a number of reasons One objection to its use is that the level must extend to the upper thoracic segments in order to secure relaxation and complete pain relief This

XXXIII

# OPERATIONS ON THE ABDOMINAL WALL, PELVIS, PERINEUM AND RECTUM

## Pelvic Surgery

Most pelvic surgery is either gynecological or urological in nature Urological surgery is discussed under that heading The bulk of pelvic surgery is performed on women most of whom are in relatively good condition They therefore present few difficult problems from the standpoint of anesthesia The operations are largely for benign disturbances caused by trauma from childbirth, infections or new growths Hysterectomy, salpingectomy, oophorectomy, plastic operations on the tubes, uterine suspensions, removal of cysts are the usual operations performed Less frequently patients in the older age group beyond the menopause come to surgery Women in this age group are usually operated upon for excision of malignant neoplasms or degenerative changes in the female pelvic organs In these, cardiovascular diseases, metabolic disturbances, and manifestations of degenerative diseases are common

The choice of anesthesia and requirements for pelvic surgery are similar to those outlined for lower abdominal surgery with perhaps one point of difference Most operations are performed in the Trendelenburg, lithotomy or Sims position Circulatory disturbances due to positional changes and interference with ventilatory movements are often noted Spinal anesthesia is satisfactory for most pelvic surgery performed in women of the younger age group It is better judgment to avoid it when large ovarian or uterine masses are excised or where pelvic inflammatory disease of an acute nature is being operated upon Intra abdominal bleeding and ectopic pregnancy, even though the patient is not in shock, is a contraindication to spinal anesthesia In the older age groups contraindications to spinal anesthesia usually exist and general anesthesia is preferred When spinal anesthesia is not desired cyclopropane alone or combined with ether may be used The combination of nitrous oxide, an ultra short acting barbiturate and a muscle relaxant is used by many but is a less desirable choice Local anesthesia and nerve blocking is rarely satisfactory It is selected for poor risk subjects undergoing urgent surgery

Radical dissections are performed with spinal anesthesia if the patient is in good condition Cyclopropane, or cyclopropane ether may be used when spinal anesthesia is not desired Thiopental and nitrous with a muscle relaxant is a less desirable choice Hypotensive anesthesia is often used if extensive bleeding is anticipated

## THE ABDOMINAL WALL

### Hernia

Operations on the abdominal wall usually consist of repairs of defects such as herniations or weaknesses of the walls, removal of benign growth or skin grafts Hernias are usually inguinal, femoral or incisional Inasmuch as most hernial sacs usually are extensions of the peritoneal cavity and the sac contains intestines, omentum and other viscera, selection and the management of anesthesia is essentially that described for abdominal surgery in which the peritoneal cavity is entered Patients may be in any age group Usually the patients are infants and children who have congenital weakness which become manifest shortly after birth, young or middle aged adult males who develop or have an aggravation of a hernia due to trauma from their occupation, and old persons whose tissues have become weakened so that herniations develop For hernias in the lower abdomen a moderate degree of relaxation is required For incisional hernia considerable relaxation is needed The peritoneal cavity must be entered when incisional, epigastric or umbilical hernia are repaired Anesthesia for incisional hernia is the same as that recommended for upper abdominal surgery

Usually subjects whose hernias result from trauma in line with their occupation are males who are in good physical condition unless the hernia is incarcerated or strangulated As a rule inguinal and femoral herniotomies are of reasonable length—between one and two hours There is no remarkable blood loss or trauma Traction reflexes from tension on the cord or peritoneum are frequent when general anesthesia is used, but absent with spinal anesthesia Laryngeal spasm is the commonest manifestation of this reflex activity Spinal anesthesia is ideal for this type of surgery in adults If not desired cyclopropane combined with a muscle relaxant may be used Ether preceded by nitrous oxide is suitable, also, if one does not choose to employ cyclopropane Basal narcosis may precede inhalation anesthesia for the patient's comfort The combination of thiopental, nitrous oxide and a muscle relaxant may be used also As a rule, local anesthesia is satisfactory in the hands of one skillful in field blocking Many operators feel that the distention of the tissues by the local anesthetic solution distorts anatomic structures and may contribute to improper repairs and subsequent recurrences In the older, particularly poor risk subjects, local anesthesia is frequently selected from necessity

The anesthetic management of patients with strangulated hernias differs little from that for abdominal operations for acute surgical emergencies It must be borne in mind that strangulation may necessitate resection of the bowel and lead to formidable surgery Symptoms of intestinal obstruction and a shock like state are often present These cases must be managed in the same manner as though intestinal obstruction were present rather than as

extent of anesthesia is not sufficient to completely abolish discomfort in the chest due to reflexes Nausea, vomiting and pain in the chest or neck occur in spite of the fact that anesthesia is "high" Hypotension occurs frequently from postural changes either before or after operation Local anesthesia, or paravertebral blocks are not satisfactory except for operations of a simple nature Nephrostomy, pyelolithotomy, transplants of ureters, removal of malignant growths involving the kidney and operations technically similar to nephrectomy are managed in the same manner as nephrectomy

## Ureteral Operations

The extraperitoneal approach is used for operations involving the upper portion of ureters The trans peritoneal is used for the lower portion When the trans peritoneal approach is used surgery is performed with the patient in the supine position, otherwise the lateral prone position is used Choice of anesthesia differs in no way from that used for *intra-abdominal surgery in* the former situation When the extra peritoneal approach is used the choice is identical to that outlined for nephrectomy

## Adrenalectomy

As in the case of nephrectomy the extra peritoneal approach is used for explorations and removal of the adrenal gland Manipulations of tumors of the adrenal gland, particularly pheochromocytomas, causes the release of adrenalin like substances and paroxysms of hypertension frequently occur Ganglionic blocking or sympatholytic agents may be needed to lower the *blood pressure during these paroxysms At the conclusion of the operation* the blood pressure may decline to shock levels Vasoconstrictor substances such as arterenol or neosynephrine may be necessary to restore the blood pressure to adequate levels Anesthetics which increase cardiac irritability, particularly cyclopropane, cannot be used in these cases Ether intratracheally preceded by nitrous oxide or ethylene and a basal of thiopental is the usual technique of anesthesia employed In view of the fluctuations in blood pressure and the severe hypotension which may result the use of spinal anesthesia is not advised The possibility of pneumothorax following inadvertent tearing of the pleura is another objection to spinal anesthesia

In children operations on the kidney, ureters or adrenal gland are best performed using ether by the closed system if suitable apparatus for pedia tric anesthesia is available or by the open drop method if it is not As in the case of the adult an endotracheal catheter is necessary to provide a patent airway when the lateral prone position is used

Operations on the bladder, seminal vessels and prostate gland are performed suprapubically and although they are extra peritoneal procedures they are considered separately under urological operations

manner as that for operations on the bladder Patients undergoing prostatectomy are without exception in the upper age group They may have or have had urinary retention Some have had a previous cystotomy because of acute urinary retention and a preliminary vasectomy in anticipation of the prostatectomy Complicating diseases such as arteriosclerosis, hypertension, heart disease, emphysema, diabetes and other diseases of advanced age are the rule rather than the exception Hemorrhage at times is a factor both during and after operation Spinal anesthesia is preferred by most urologists for prostatectomy Hypertension, arteriosclerosis, coronary artery disease, if severe, may be contraindications to spinal anesthesia Under such circumstances cyclopropane, cyclopropane ether, or the combination nitrous oxide, a basal of thiopental and a muscle relaxant is used Local anesthesia is not satisfactory

The choice for *retropubic prostatectomy* is similar to that recommended for suprapubic operations *Perineal prostatectomy* is performed with the patient in combined lithotomy and Trendenlenburg position Spinal anesthesia is preferred by most surgeons but general anesthesia provides greater comfort for the patient Cyclopropane, nitrous oxide ether or nitrous oxide-thiopental may be used Caudal block and local anesthesia are not satisfactory

### Transurethral Surgery

Partial resection of the prostate transurethrally is usually performed in the lithotomy position, in a darkened room, by means of a high frequency current A fire hazard thus exists Spinal, caudal block, or the combination of thiopental and nitrous oxide are used When caudal anesthesia is used attempts to have the caudal high should be made because the bladder is distended with water which causes discomfort *Cystoscopy* and other intravesical manipulations which are performed transurethrally are managed in the same manner

### Operations on the Scrotum and Penis

Operations upon the scrotum of a minor nature such as *vasectomy*, biopsies, removal of benign growths and so on may be performed with local anesthesia For major procedures such as reduction of *hernias*, removal of *hydroceles* of the cord, *orchidectomy* or *orchidopexy* spinal anesthesia is preferred by most urologists When no contraindication to its use exists it is the most satisfactory Cyclopropane, ether or thiopental combined with nitrous oxide may be used if spinal anesthesia is undesirable or is contraindicated Local anesthesia is not suitable, as a rule, because troublesome traction reflexes are initiated by manipulation of the spermatic cord Caudal block may be used but anesthesia is not adequate for manipulations about the frenulum or dome of the bladder or to obtund traction reflexes unless the extent is "high"

hernioplasties The selection of anesthesia should be that recommended for intestinal obstruction as mentioned in the section on intra abdominal surgery Anesthesia for epigastric, incisional and umbilical hernias is similar to that recommended for upper abdominal surgery than lower

## GENITO URINARY TRACT

Urological operations on the bladder, prostate, seminal vesicles and urethra are performed suprapubically, retropubically or through the perineal route Operations on the bladder, prostate and seminal vesicles are performed by the suprapubic route Bladder operations involve partial or complete resections, removal of new growths, decompressions, drainages, removal of diverticulae and excision of fistulae Operations on the prostate gland are largely enucleations Operations on the external genitalia consist of vasectomy, orchidectomy, hydrocelectomy, circumcision, Torek operation and various other plastic procedures

### Cystotomy

Cystotomy is performed for relief of urinary retention, removal of new growths, diverticulae, etc The majority of patients are in the older age group The usual route for operation on the bladder is suprapubically and extra peritoneally Relaxation of the lower recti is necessary to expose the pelvic structures, when these approaches are used Most urologists prefer spinal anesthesia for bladder surgery However, cyclopropane, ether, or nitrous oxide and a basal narcotic combined with a muscle relaxant may be used with equal efficacy

### Cystectomy

Anesthesia for cystectomy is managed in the same manner as that for other lower intra abdominal or pelvic operations If no contraindications exist spinal anesthesia is satisfactory If spinal anesthesia is not desired or is contraindicated, cyclopropane or nitrous oxide combined with ether may be used The combination of nitrous oxide, a basal of thiopental and a muscle relaxant may be used Cystectomies are not easily performed under local anesthesia Traction reflexes, though not as troublesome as those arising during intraperitoneal explorations, are encountered Cystectomy may be difficult and time consuming depending upon the contour of the pelvis The duration of the operation of course varies with circumstances, the skill of the surgeon and other variable factors Several hours at least may be required to complete the operation

## OPERATIONS ON MALE REPRODUCTIVE ORGANS

### Prostatectomy

Prostatectomy may be performed by the suprapubic, retropubic or perineal routes Anesthesia for suprapubic prostatectomy is managed in the same

CLINICAL RECORD — ANESTHESIA

gastrectomy

☒ GOOD ☐ FAIR ☐ POOR

morph 1/4 scop 1/100

PREMEDICATION

INDUCTION

MAINTENANCE

ENDOTRACHEAL

RECOVERY

ETHER

PLANE OF THE STAGE 1 2 3 4

180 160 140 120 100 80 60 40 20

● PULSE

○ RESP

∨∧ B.P.

× RES.

⊙ OPER.

traction

atropine

SUPPORTIVE TREATMENT

DETAILS OF REGIONAL OR SPINAL

POSTURE supine

DRAINS

OPERATION PERFORMED gastrectomy

PRIMARY AGENT ether

SECONDARY AGENT

SIGNATURE OF ANESTHETIST

VA FORM 10-2614g-2 — ANESTHESIA

Fig 34 Hypotensive state showing the changes in pulse and blood pressure which arise when traction is made upon the viscera or when the peritoneal structures are stimulated Note the bradycardia the narrowed pulse pressure the lowered systolic and fairly well maintained diastolic pressure Sympathomimetic amines or anticholinergic drugs are usually effective in overcoming this hypotensive state

### Circumcision and Other Penile Operations

Circumcision in adult patients is performed with local anesthesia as a rule Spinal anesthesia is a major anesthetic for a relatively minor procedure but may be used also In children it is customary to use ether or cyclopropane for circumcision Thiopental is not suitable, because stimulation of the penis causes laryngeal spasm by reflex stimulation, and priapism

*Amputation of the penis* is performed with spinal anesthesia if there is no contraindication, otherwise cyclopropane, or ether are used *Plastic operations* on the external genitalia are performed with local anesthesia if minor in nature Spinal anesthesia is used for the more extensive longer procedures Where topical anesthesia is contraindicated, ether or cyclopropane may be used

## PERINEAL OPERATIONS ON THE FEMALE GENITALIA

Perineal operations involving the external female genitalia and vagina are usually performed in the lithotomy or Sims position The airway is easily managed from the standpoint of anesthesia in either case All ages are represented However, most operations of this type consist of plastic repairs and are performed in women in the younger age group Women of the older age group are encountered when malignant tumors are present Reflexes from manipulation of perineal structures cause circulatory changes and disturbances of the respiratory pattern Laryngeal spasm is common when general anesthesia is used Often the blood pressure falls These hypotensive states differ from shock from trauma or hemorrhage in being characterized by a bradycardia, a low systolic, normal diastolic and a narrowed pulse pressure (Fig 34) Blood loss is not great in this type of surgery Relaxation is not required as a rule

*Perineorrhaphy, anterior* and *posterior repairs, operations on the cervix, cauterizations, vulvectomy, excision of cysts* and so on may be performed satisfactorily with low spinal anesthesia Inhalation anesthesia using cyclopropane, ethylene or ether or the combination of thiopental, nitrous oxide and a muscle relaxant may be used when spinal anesthesia is not desired or is contraindicated Local or caudal anesthesia is not satisfactory as a rule for this type of surgery because the fundus of the uterus and the area about the clitoris is not anesthetic unless the caudal is "high"

*Vaginal hysterectomy* is a frequently performed operation More profound and extensive anesthesia is required than is usually provided for this operation Relaxation of the abdominal muscles is necessary, otherwise the patient forces the pelvic contents into the vagina by the contraction of the recti which is initiated by stimulation of the peritoneum When spinal anesthesia is used it must extend to at least the 8th thoracic segment for complete abolition of pain

Inasmuch as most gynecological surgery is performed in the lithotomy

# XXXIV

# OPERATIONS ON THE VERTEBRAL COLUMN AND EXTREMITIES

## VERTEBRAL COLUMN

Operations on the vertebral column consist of laminectomies, spinal fusions, explorations of the spinal cord for tumors and ruptured intervertebral disks, chordotomy, transections and so on Laminectomies may be cervical, thoracic or lumbar Some patients may have paralysis and other neurologic symptoms in the lower part of the body, others paralysis of the respiratory muscles requiring an iron lung Bony changes due to tuberculosis or arthritis may be present Some are performed for fractures or other lesions due to trauma Shock may be present in these All surgery on the vertebral column, with few exceptions, is performed in the prone position Operations about the vertebral column are usually long, tedious and may be accompanied by shock and blood loss Most surgeons use the electro surgical unit for securing hemostasis by coagulation This creates a fire hazard Inasmuch as the prone position is mandatory, interference with respiratory exchange and difficulty in maintaining an airway are frequent Circulatory changes, usually a hypotension, follow the changes from one position to the other

Operations upon the cervical and thoracic portion of the vertebral column must be performed under general anesthesia Local anesthesia is not suitable The combination of nitrous oxide and a basal of thiopental is used most often when a fire hazard exists, otherwise cyclopropane, ether, or ethylene or nitrous oxide ether may be used An endotracheal catheter must be used to allow the anesthetist to be out of the operative field and still maintain an adequate airway When the operation is being performed upon the lumbar vertebrae, sacrum or coccyx, spinal anesthesia may be used for subjects in whom it is not contraindicated, otherwise the procedure is as outlined for thoracic and cervical laminectomy

## THE EXTREMITIES

Operations on the extremities involve the forearm, arm, shoulder, hand and digits in the upper part of the body and the hip, leg, ankle, foot, and toes on the lower Lesions encountered are the result of trauma, infections, malformations and new growths Trauma and infection are the basis for the lesions for which the majority of procedures are performed since they give rise to deformities requiring reconstructions and plastic procedures Amputations, reduction of fractures, skin grafts, tendon transplants, incision

position, problems concerning the airway arise less frequently because the head is accessible to the anesthetist Obese subjects only, need be intubated Some operators prefer the Sims position This is awkward as far as main taining an adequate airway is concerned Endotracheal anesthesia is neces sary most of the time if this position is employed

## RECTAL OPERATIONS

Hemorrhoidectomy is the most common rectal operation Repair of pro lapse, imperforate anus, removal of fistulae, excision of fissures are less com mon Protoscopic examination usually requires no anesthesia Rectal opera tions require relaxation of the sphincter and perineal muscles The lithotomy position is used for rectal surgery This is of no handicap to the anesthetist as far as the airway is concerned Some surgeons prefer the prone or the Buie position in which case the airway is maintained with difficulty From the standpoint of comfort and safety to the patient a low spinal or saddle block is the best choice for rectal surgery It provides the relaxation that the surgeon requires

A cautery is frequently used for rectal surgery by some surgeons neces sitating a non flammable anesthetic Spinal and caudal anesthesia satisfy this requirement Inhalation anesthesia with cyclopropane or ether is suita ble when spinal or caudal anesthesia are not desired or is absolutely con traindicated which is not often In view of the difficulty in maintaining the airway use of an endotracheal tube is advised if general anesthesia in the prone position is used Barbiturates with nitrous oxide are a less desirable choice, primarily because of the spasmogenic nature of the barbiturate and the ease with which spasm is initiated by dilating the rectum Nitrous oxide, ethylene and other anesthetics are not suitable because they do not provide adequate relaxation Some surgeons perform minor surgery in the rectal area using local anesthesia but as a rule it is not satisfactory

Rectal operations on children are best performed with general anesthesia Ether by the open drop method is the usual choice If suitable apparatus is available the closed system is used Endotracheal intubation may be needed to maintain an adequate airway

### REFERENCES

ADRIANI JOHN ROMAN D A Saddle block anesthesia *Am J Surg 71* 12–18, 1946

DYE F C VAUGH J A Hypobaric saddle block anesthesia for surgery *Anesthesiology, 10* 489 1949

MARTIN S J FEENEY T M Anesthesia in pediatric urology *J A M A 148* 180–184 1952

TUOHY E B Regional anesthesia for operations on perineum annus genitalia and lower extremities *Anesthesiology 2* 369–388 1941

WILKINSON F A H Nupercaine spinal anesthesia for abdomino perineal resection of rectum *Anesthesiology 3* 437–445 1942

propane is ideal Ethylene combined with ether may be used The thiopental, nitrous oxide combination likewise is satisfactory

Operations on the *hand* may be performed using brachial plexus block or the combination of median ulnar and radial nerve blocks at the elbow or wrist If the lesion is localized and not extensive, local infiltration is often used For operations on the *fingers*, brachial plexus block or digital block may be used When general anesthesia is desired nitrous oxide, ethylene, cyclopropane, the combination of nitrous oxide and thiopental are all satisfactory depending upon the preference of the operator and the duration of operation It cannot be emphasized too strongly that for operations on the digits, epinephrine is best omitted when local anesthesia is used Vasospasm followed by gangrene may result if peripheral vascular diseases are present

## Hip

Operations on the *hip* are best performed with either a low spinal or some form of general anesthesia Relaxation is an essential requirement Nerve blocking is not satisfactory as the number of nerves to be blocked are numerous and not easily accessible Cyclopropane is ideal for this type of surgery If it cannot be used alone the combination of cyclopropane-ether is employed Nitrous oxide, and thiopental likewise may be used as can ethylene or nitrous oxide followed by ether For children open drop ether with a preliminary of vinyl ether may be used if suitable closed system apparatus is not available, otherwise ether or cyclopropane by the closed system may be used

## Leg, Ankle and Foot

General anesthesia for operations on the leg, ankle, foot and toes is similar to that selected for operations on the thigh Where regional anesthesia is desired for *operations below the knee*, a combination of femoral and sciatic nerve block is satisfactory Operations on the *foot* may be performed by blocking the anterior tibial, posterior tibial, sural and saphenous nerves at the ankle Digital blocks may be used for operations on the *toes* Epinephrine should be omitted, otherwise vasospasm may lead to gangrene of the members

### Anesthesia for Thigh and Leg Amputations

Mid thigh, leg and foot amputations are operations which are being performed with increasing frequency largely due to the fact that the number of geriatric patients is increasing The majority of amputations are for peripheral vascular disease, particularly arteriosclerosis Diabetes is usually associated with the vascular disturbance Traumatic lesions, skeletal defects and infections of bones and joints account for a much smaller percentage of amputations When the amputation is for trauma the patient may be in

and drainage of abscesses are some of the more common operations encountered However this does not in any way enumerate all the possible procedures encountered

Some operations are considered under the category of minor surgery and are performed using nerve block or local infiltration Others are formidable, prolonged, and require general anesthesia In the management of anesthesia for surgery of the extremities, consideration must be given to the duration of the operation, the necessity for relaxation, blood loss, trauma and so on The supine position is used almost always The airway is easily maintained except in the obese or in patients with abnormalities of the respiratory passages Patients range from infants to the extremely old Operations about the shoulder girdle and clavicle may require the use of endotracheal anesthesia at times particularly if the operator must stand at the head Otherwise the ordinary mask technique may be used Shock and hemorrhage may be complications of bone surgery

For surgery of the arm or leg a tourniquet is often used Skin grafting may require removal of skin from the abdomen or other areas other than the extremity The graft may be applied to the operative site in the extremity with regional anesthesia but general anesthesia may be needed to obtain the graft Muscle relaxation is a requisite in orthopedic procedures of the arm or thigh or the forearm and calf Rarely is it a problem in operations on the feet, toes, fingers, foot, or hand

## Operations About the Shoulder and Arm

General anesthesia is best for most operations about the shoulder Moderate to extreme muscle relaxation may be required Anesthesia may have to be, as a rule, deep Nerve blocking is not satisfactory For minor superficial operations local anesthesia may be used Cyclopropane or cyclopropane ether are ideal for this type of surgery Where cyclopropane is contraindicated nitrous oxide or ethylene followed by ether may be used For short procedures or for procedures in which the cautery is required thiopental and nitrous oxide may be used Vinyl ether may be used for children when the procedures are short Open drop ether is used in longer cases Where suitable apparatus is available for using closed system anesthesia, selection and management for children is identical to that used for adults

## Forearm

Operations on the *forearm* or elbow may be performed using a brachial plexus block Where this is not desired or suitable, cyclopropane or ethylene and ether or the combination of cyclopropane ether, nitrous oxide with thiopental may be used Operations on the *wrist* may be performed with a combination of median, ulnar or radial nerve block performed on the elbow or better yet brachial plexus block When general anesthesia is required cyclo-

# XXXV

# AUTONOMIC NERVOUS SYSTEM, SKIN AND BLOOD VESSELS

## AUTONOMIC NERVOUS SYSTEM

Operations on the autonomic nervous system are largely confined to the removal of sympathetic ganglia and vagotomy Vagotomy is described in the section on gastric surgery Lumbar sympathectomy is the most common of the operations on the sympathetic nervous system The stellate, thoracic, and presacral ganglia are also removed but less frequently Also associated with sympathectomy is adrenelectomy This has been discussed in chapter (XXXIII)

Operations on the autonomic nervous system are performed for *intractable pain* which is mediated along the sympathetic fibers Various types of causalgia, the relief of angina, and pain involving the pelvic organs are the most frequent syndromes involved In addition sympathectomy is performed to attempt to *lower the blood pressure* in malignant hypertension, and to relieve vasospasm of the arm or leg, in cases of peripheral vascular disease in which gangrene is impending

The status of the patient for sympathectomy is influenced to a great extent by the disease for which the ablation of the autonomic nervous system is being performed This should yield sufficient and important clues in evaluating the patient

*Stellate ganglionectomy* is usually performed to relieve pain of cardiac origin, pain in the head of the causalgic type or for vasospastic disease of the upper extremities Regional anesthesia is not satisfactory, general anesthesia must be used The operation is usually performed with endotracheal anesthesia because the surgeon and the anesthetist both compete for the operative field The airway cannot be under adequate control without it Cyclopropane, ethylene or nitrous oxide followed by ether may be used The combination of nitrous oxide and thiopental may be used if a cautery is required It must be remembered that the pleura may be pierced and pneumothorax may result during this operation As a rule, except when the operation is performed to relieve cardiac pain, the majority of these patients are in good condition and are good surgical risks

*Thoracic sympathectomy* is usually performed in combination with lumbar sympathectomy for relief of malignant hypertension Cardiac and renal involvement may be present A severe hypotensive state may develop during or at the conclusion of the operation The operation must be performed

any age group Shock may be or may have been a factor before surgery Sepsis and fever may be factors when infection is present In older patients, cardiovascular and renal disease may be present

For patients in good physical condition with no cardiovascular disturbances and normal blood volume, low spinal anesthesia is ideal If general anesthesia is desired, cyclopropane or cyclopropane-ether is suitable Ethylene-ether, nitrous oxide-ether or nitrous oxide-thiopental may be used Refrigeration anesthesia may be used for poor risk subjects if the operating time is less than 30 minutes and a tourniquet is not objectionable For extremely poor risk subjects in whom amputation cannot be performed promptly the limb may be packed in ice after application of a tourniquet and operation deferred for hours until the patient can be properly prepared This is equivalent to a physiologic amputation Marked improvement in status often results Later the operation may be performed with cyclopropane or ether Nerve blocks as a rule are not satisfactory for amputations particularly in the mid and upper thigh Sciatic, femoral obturator and lateral femoral cutaneous nerve blocks would have to be combined to obtain satisfactory anesthesia Local infiltration is not satisfactory Muscle relaxants are not necessary for this type surgery

REFERENCES

ALLEN F M Refrigeration anesthesia for lumbar operations. *Anesthesiology*, 4 12–17, 1945

HUNTER A. R. Anesthesia for operations on the vertebral canal *Anesthesiology 11* 567–575 1950

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using the transthoracic approach usually in the lateral position The problems are those of open chest surgery Endotracheal anesthesia is required to facilitate controlled breathing and maintenance of the airway The anesthetic management for this type of surgery is similar to that outlined for stellate ganglionectomy

In exposing the lumbar ganglia relaxation of the lumbar and abdominal muscles is required for adequate exposure Deep anesthesia is needed After the ganglia are removed the blood pressure may decline, often abruptly, to shock levels Measures must be instituted to combat extreme degrees of hypotension The operation is not one of long duration as a rule When lumbar sympathectomy alone is performed the patient is usually placed in the semi lateral position Spinal anesthesia provides the needed relaxation and is preferred except for extreme degrees of hypertension with serious cardiac involvement Cyclopropane ether intratracheally, or nitrous oxide thiopental with a muscle relaxant may be used when spinal anesthesia is contraindicated Nerve blocking is not satisfactory

*Presacral neurectomy* is performed for pain of visceral origin in the lower abdomen or pelvis It is usually associated with gynecological surgery A transabdominal approach is used to excise the ganglia Anesthesia, therefore, differs in no way from that required for pelvic surgery The selection is similar to that used by gynecological laparotomies

## SKIN

Surgery of the skin consists of skin grafts, removal of moles and similar growths and management of burned patients Anesthesia for skin grafts and excision of cutaneous lesions is discussed under the various sections of the body such as head neck, thorax and so on The management of the burned patient will be discussed subsequently

### Anesthesia for the Burned Patient

Fresh burns occasionally require anesthesia for cleansing and debridement of burned and necrotic tissues Extensively burned patients are poor risks They may be dehydrated, have an extreme degree of hemoconcentration and often are in shock The debridement should be performed without anesthesia, whenever possible to do so However if anesthesia is required, one which is labile, allows a high oxygen tension and rapid recovery with as little disturbance of metabolic functions as possible is desirable Cyclopropane meets these requirements Ether is not desirable because of the after effects such as nausea and vomiting the slow elimination and the effects on blood volume Non volatile drugs should be avoided because of the prolonged depression Liver and kidney functions may be disturbed in patients with burns which further precludes the use of the non volatile drugs These drugs are not easily detoxified under these circumstances If

a narcotic has been given for pain ethylene or nitrous oxide may be used to fortify its effect when analgesia only is required When the face is burned and a mask cannot be applied topical anesthesia is used and the patient is intubated "awake" after which anesthesia is managed in the usual manner

Patients whose burns have been long standing may require anesthesia for removal of dressings, debridements and for applying skin grafts The physical status of these patients may be variable depending upon the duration and severity of the burn Signs of sepsis and anemia may be present Renal and liver impairment, emaciation, weight loss, effects of impaired nutrition may all be present after extensive burns During surgery "weeping" from the raw surface may result in considerable blood loss Hypotension from trauma in grafting may result also Operations for skin grafting are often long and tedious and require considerable time Blood should be administered during the operation

For removal of dressings analgesia is sufficient Nitrous oxide alone may be used A combination of nitrous oxide and trichlorethylene or vinyl ether administered with a semi-closed inhaler operating on the demand principle is highly satisfactory Premedication is not necessary for these cases Trichlorethylene or vinyl ether alone may be used but are less satisfactory

When the procedure is extensive and involves debridement and grafting general anesthesia is desired analgesia is not sufficient Cyclopropane is the best choice because it is labile and followed by rapid recovery Besides it disturbs blood volume and metabolic processes so little Less desirable are ethylene or nitrous oxide ether mixtures or the thiopental nitrous oxide combination When the face is burned an endotracheal tube is introduced while the patient is conscious using topical anesthesia, and then anesthesia is managed in the same way

## BLOOD VESSELS

Operations on the blood vessels consist of excision of aneurysms closure of fistulae, ligations, embolectomy, or injection of a dye to visualize the vessel radiologically With the exception of angiography these have been discussed along with surgery of the heart or extremities

### Anesthesia for Angiography

Angiography frequently requires anesthesia for successful completion Visualization of the vessels in the cerebrum, neck, the kidney and the pelvic organs is often attempted When a cerebral angiogram is attempted the opaque medium is injected into the carotid arteries When the chambers of the heart and vessels of the lungs require visualization the arm vein is used or a catheter is placed into the vein in the arm and guided into the right auricle For performing renal angiograms and visualization of the pelvic vessels the dye is placed in the aorta Cardiac catheterization is

performed to study the blood gas composition in the chambers of the heart in certain cardiovascular diseases These procedures are performed in the X ray room often in the dark A fire hazard exists

Local anesthesia is used for angiograms of the head to expose the carotid artery If local anesthesia is not satisfactory, thiopental combined with nitrous oxide supplemented with local is the usual choice Usually no anesthesia is required for adults for thoracic angiograms For children general anesthesia is mandatory due to lack of cooperation Vinethene-ether is satisfactory or thiopental nitrous oxide is used if a fire hazard exists For angiograms in the lower extremities, spinal anesthesia or thiopental combined with nitrous oxide may be used for adults Thiopental nitrous oxide is used for children

*Cardiac catheterization* must be performed with non volatile drugs because the specimens of blood must be devoid of anesthetic gases to insure accurate analysis Local anesthesia at the site of puncture is used for introducing the catheter A basal consisting of an ultra short acting barbiturate, usually thiopental rectally or intravenously, is used to obtain a general hypnotic effect

## REFERENCES

BEECHER H K Resuscitation and sedation of patients with burns *Am J Surg 117* 825 1943

CLARK S S Anesthesia for thoracolumbar sympathectomy *Anesthesiology 11* 345–350 1950

KUNTZ A *The Neuroanatomic Basis for Surgery of the Autonomic Nervous System* Springfield Thomas 1952

MANSEL L H Anesthetic management of patients during vagotomy dorsal ympathectomies etc *South M J*, *41* 702–712, 1948

PHELPS M L BURDICK D L Anesthetic management of patients undergoing sympathectomy *Anesthesiology 4* 361–371 1943

ROVENSTINE E A CULLEN S C Anesthetic management of patients with hyperactive carotid sinus *Surgery 6* 167–176 1937

SMITHWICK R *Surgical Measures in Hypertension* Springfield Thomas, 1952

# XXXVI

# ANESTHESIA FOR OBSTETRICAL PATIENTS

## Differences Between Anesthesia for Obstetrics and for Surgery

Although responsibility in anesthesia is great at all times it is still greater when dealing with the obstetric patient This is so because two individuals are involved instead of one Then, in addition, the usual obstetric patient is one who is young, vigorous, and in good health with her life ahead of her to say nothing of the future of the expected child Besides the anesthetic is administered to complete a normal physiologic process instead of correcting a pathologic condition

Obstetrical anesthesia at times is simple, and other times complex Unfortunately, too often it is regarded lightly and its administration is relegated to inexperienced persons The two individuals who are involved, behave differently from a physiologic standpoint The reactions of the fetus to anesthetic drugs are unpredictable Much depends upon whether or not the child is at term or is premature Responses to disturbances in gaseous exchange, drugs, blood loss, trauma, or reflex stimulation may differ according to the age of the fetus

In obstetrics one must be prepared to deal with a common agent and technique for both the mother and child Consideration must be given to complications of pregnancy and problems of abnormal labor The anesthetic management usually presents no difficulty in normal obstetric cases as far as the mother is concerned because the majority of women in the child bearing period are in good physical condition It is in the abnormal cases that difficulties are encountered, however Pre-existing medical diseases involving the respiratory, cardiovascular, renal hepatic and neurologic systems may be aggravated by pregnancy Anesthesia must be selected accordingly In addition to these, the "medical" complications of pregnancy may be present Toxemia, nephritis and hypertension are the conditions most often encountered Electrolyte disturbances usually expected in pregnancy may be enhanced by dehydration, anoxia or vomiting during or prior to labor

During the delivery the anesthetist is concerned with the possibility of aspiration of vomitus Deaths from asphyxia during or after general anesthesia for delivery are preventable and inexcusable Food and drink should be withheld in all patients to be delivered with general anesthesia whenever possible No surgeon would permit his patient to partake of food prior to an elective operation The situation is no different in obstetrics Too many obstetricians, even though they expect to use general anesthesia

for delivery, allow patients to have food during labor completely oblivious of the hazard to which the patient will be exposed There is little that one can do to avoid aspiration once vomiting occurs There is no assurance that aspiration will not occur irrespective of the measures one initiates after regurgitation begins Prevention is better than cure

Other problems which may arise of concern to the anesthetist are post partum hemorrhage from uterine inertia and lacerations of the cervix or uterus Shock may occur from trauma, instrumentation, rupture of the uterus, long labor and so on

## Requirements for Pain Relief

There are two phases of analgesia and anesthesia for obstetrics (1) Providing amnesia and analgesia during labor up to the point of delivery and (2) anesthesia for the delivery Analgesia must be such that it does not interfere with labor Anesthesia at the time of delivery is actually surgical anesthesia It cannot be emphasized too strongly that it differs in no way from surgical anesthesia in regards to depth, technique and hazards It is often administered without the benefit of premedication, which of course, makes it still more difficult and hazardous In general the preparation and conduct are the same as for a surgical operation An anti cholinergic drug should be administered 30 to 45 minutes prior to anesthesia to prevent formation of secretions This should be administered intravenously in urgent cases when there is insufficient time for the effects to be established by the subcutaneous route

## Analgesia for Labor

The type of analgesia for labor varies with the individual preferences of the obstetrician In current day practice, what is referred to as analgesia is largely hypnosis and amnesia The barbiturates administered alone with no other drug provide no pain relief The barbiturates combined with nar cotics provide some analgesia and are preferred to the barbiturates alone These combinations seem to be popular in present day practice Usually a combination of meperidine, secobarbital or pentobarbital and scopolamine induces a satisfactory degree of amnesia and analgesia Nitrous oxide oxygen (80 20%) administered intermittently during the uterine contractions en hances the effects of the narcotic and yields a high degree of analgesia Nitrous oxide unfortunately has not been properly used for analgesia and for this reason has fallen into disuse If administered at the height of the contraction, as is often done, instead of at the beginning, its analgesic effect becomes es- tablished as the contraction is receding (Fig 35) The apparatus should be readied with the breathing bag filled with the mixture As soon as the patient experiences the sensation of a beginning contraction the mask is applied to the face and she is instructed to inhale deeply several times

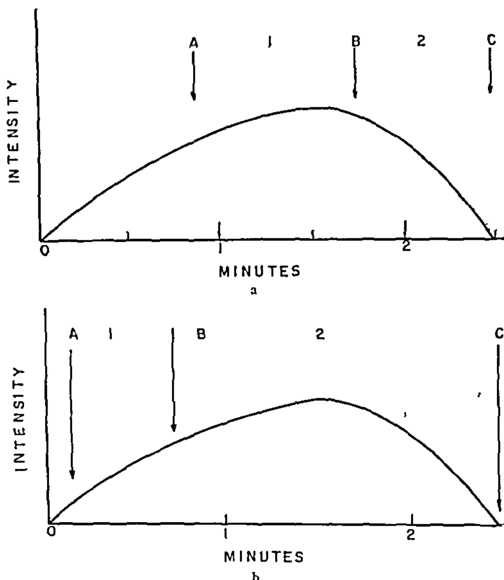



FIG 35 The establishment of analgesia using nitrous oxide during labor At least 20 seconds elapse (zone 1) before effective analgesia is established (zone 2) This is after the peak of the contraction has been reached if the administration (A) of the gas is delayed until the patient begins to complain of pain (a) The effective zone of analgesia is established before the height of the contraction is attained if the inhaler is filled with gas and held in readiness and administration is commenced as soon as the patient senses the onset of a contraction (b)

Analgesia is established before the height of the contraction is reached if this procedure is followed

Trichlorethylene has recently been popularized and may also be used intermittently Devices for self-administration such as the Cyprane or Duke inhaler are available Ethylene may be used instead of nitrous oxide and in the same manner Cyclopropane is more potent, causes nausea, and is not without hazard Intravenous procaine, intravenous alcohol, rectal ether, and paraldehyde have been claimed as excellent by enthusiasts but as a rule leave much to be desired and are little used Caudal and saddle block may be used for analgesia when the use of systemic depressants is not advised Cutaneous infiltration over the abdomen and sympathetic blocks are usually not satisfactory

## Anesthesia for Delivery

Two types of patients must be considered for anesthesia for delivery in uncomplicated obstetrics, the primipara and multipara The primipara as a rule undergoes a longer period of labor and requires an instrumental delivery with an episiotomy More profound anesthesia is required under these circumstances than ordinarily Multipara ordinarily do not require an episiotomy or the use of forceps Less profound anesthesia of briefer duration is required When forceps are used or an episiotomy is performed the anesthetic management differs in no way from that of a primipara When operative obstetrics is to be performed, such as a version, a craniec tomy, high forceps and so on, surgical anesthesia must be provided For a version the anesthetic must be of such a depth to relax the uterus completely A rapid acting anesthetic is invaluable for urgent situations such as prolapse of the cord, precipitate labor and so on

Inhalation anesthesia is the best choice when general anesthesia is desired to complete a normal delivery When analgesia with nitrous oxide and a barbiturates has been used during labor, cyclopropane is ideal for the delivery particularly when forceps are used and episiotomy is performed If instrumentation is not necessary and lighter anesthesia may be used, ethylene or nitrous oxide are satisfactory It cannot be emphasized too strongly that the nitrous oxide or ethylene must be administered in non asphyxial concentrations without anoxia When they cannot be administered without sub oxygenation, they should be fortified with some other drug such as vinyl ether, trichlorethylene or ethyl ether For this reason, cyclo propane is preferred for anesthesia as it requires no fortification and anoxia is no problem It is rapid acting, labile and depth may be varied as required

Cyclopropane also is the anesthetic of choice for operative obstetrics because it is labile and permits one to use light or deep anesthesia as the requirements of the case may be When cyclopropane is not desired or is contraindicated ethylene or nitrous oxide fortified with ether may be used Nausea, of course, cannot be avoided with ether Deep ether anesthesia should be used to obtain relaxation of the uterus for versions Chloroform is used by some but its cardiac effects cannot be ignored Muscle relaxants have no effect on smooth muscle and do not relax the uterus, and are, therefore, useless There is little or no indication for the use of muscle relaxants in obstetrics The tissues of the birth canal are stretched by passage of the fetal head Obviously, since these tissues are not composed of striated muscle, they are not affected by the muscle relaxants

All the currently used central nervous system depressants, both volatile and non volatile, and the muscle relaxants pass through the placental mem brane The elimination of the volatile anesthetics in the new born occurs in exactly the same manner and follows the same physical laws as their elimination in adults The new born is also narcotized by the drug as is

the adult Recovery of the new born as in the case of the mother is most rapid after nitrous oxide and ethylene, next after cyclopropane and longest after ether

The use of non volatile drugs for anesthesia for delivery is not advised because they usually cause depression of respiration Thiopental is used as an anesthetic for delivery by few obstetricians If used for deliveries lasting more than 4 or 5 minutes the drug passes into the fetal circulation in sufficient quantities to cause respiratory distress after delivery For brief procedures, their use might be justified when combined with an analgesic substance such as nitrous oxide Thiopental used alone for obstetrics behaves in exactly the same manner as it does for surgical operations The barbiturate is spasmogenic As the head passes over the perineum severe laryngeal spasm may be initiated by reflex stimulation For this reason barbiturates, particularly thiopental and surital, are best avoided In long obstetric procedures and in Caesarean sections, their use is certainly not advised

Spinal anesthesia may be used in obstetrics as terminal anesthesia for delivery Low spinal anesthesia or saddle block is satisfactory in cases of normal deliveries where there is no disproportion between pelvic outlet and the fetal head, no malrotation or where hemorrhage is not anticipated Hypotension may occur, but if anesthesia is confined to the sacral segments it is uncommon and can be easily corrected with vasopressor drugs The pregnant female responds to spinal anesthesia in the same manner as do other patients with increased abdominal pressure In blocks which extend into the lumbar and thoracic segments the hypotension may be severe due to a decrease of the venous return to the heart caused by compression of the abdominal veins The fall in blood pressure may be precipitous and does not readily respond to vasoconstrictors under these circumstances The blood pressure rises as soon as the delivery is complete Spinal anesthesia in the hands of a competent, careful anesthesist who observes the patient constantly is reasonably safe for obstetrics, including Caesarean section

Caudal block by the single injection or continous technique likewise is satisfactory if performed by one familiar with the details and all the advantages and drawbacks of the method Hypotension is also a possibility when caudal anesthesia is used Pudendal block and local infiltration may be used for delivery in patients in whom general anesthesia is not desired or contraindicated Few who attempt blocks are sufficiently skilled in the technique to obtain invariable success In most instances patients prefer general anesthesia Regional anesthesia is desirable from the standpoint of the child because there is no respiratory depression

The problem of anesthesia for operative obstetrics or cases in which an obstetric complication exists may require special consideration Breech deliveries require immediate rapid induction and relaxation Cyclopropane

followed by ether if relaxation is not adequate, may be used Uterine contraction rings require deep ether anesthesia to relax the uterus Anesthetics which do not relax smooth muscle such as ethylene, cyclopropane, nitrous oxide, caudal or saddle block are not satisfactory Anesthesia for delivery of twins or triplets differs in no way from that for normal delivery When prolapse of the cord exists and speed is essential as well as profound anesthesia cyclopropane has no equal Delivery complicated by rupture of the uterus, placenta previa etc is usually by Caesarean section Anesthesia is managed as described under that heading

## Anesthesia for Caesarean Section

The type of anesthesia to be used for Caesarean section is governed by the status of the patient both obstetrically and otherwise A Caesarean section is a surgical procedure and must be managed accordingly In addition the baby has to be considered Cyclopropane is the best choice because of its lability, its relaxing power and the adequate oxygenation it affords Unlike nitrous oxide or ethylene it is devoid of asphyxial qualities When it cannot be used or when it is not desired, ethylene or nitrous oxide fortified with ether may be used It must be remembered that in obstetrics, the longer an anesthetic is administered, the greater the quantity of drug which passes into the fetal circulation Therefore, when ether is used for Caesarean section for fifteen or twenty minutes before delivery, the new born will be anesthetized and may require considerable time to "awaken "

The combination of thiobarbiturates, muscle relaxants and nitrous oxide may be used in circumstances in which the operator works quickly and deftly As a rule it is undesirable for the obvious reason that it is difficult to minimize the amount of non volatile drug used Muscle relaxants are rarely necessary for Caesarean section as relaxation is no problem The abdominal wall is so relaxed that closure is easy Local anesthesia is preferred and has been strongly advocated by many obstetricians for Caesarean section Others prefer local anesthesia until the moment of delivery and then narcotize the patient with an ultra short-acting barbiturate (thiopental) or a general anesthetic (cyclopropane or ether) This is a permissible procedure as it protects the new born Spinal anesthesia has its advocates The hypotension is the only drawback Caudal anesthesia and saddle block do not provide sufficient area of anesthesia The level must extend to the xiphoid

## Anesthesia and Medical Complications of Obstetrics

Probably the most vexsome complication encountered in obstetrical patients is toxemia of pregnancy Ordinarily if the toxemia is mild ' and there is no serious elevation in blood pressure the choice of anesthesia is no problem Cyclopropane may be used most of the time Ethylene or nitrous oxide combined with ether may be used when cyclopropane is not desired Objection

could be raised to the use of ether because of its supposed effect on liver function Obviously an anesthetic which elevates the blood pressure is not desired where hypertension exists Cyclopropane is avoided because it elevates the blood pressure There is no objection to a cautious trial of cyclopropane and change over to ether or some other agent if the blood pressure does rise Drugs which cause a hypotension are not desirable Spinal anesthesia is objectionable from this standpoint Caudal block is less apt to cause a fall, but may do so also

Inasmuch as the non volatile drugs are detoxified by the liver and their elimination is unpredictable their use is not advised Their use in any excessive quantity may cause prolonged depression in the postdelivery period When they have been used to control convulsions, the basal narcosis they provide facilitates inhalation anesthesia Ethylene or nitrous oxide may then be used as complimental agents Wherever doubt exists, particularly when the blood pressure is elevated, local anesthesia or pudendal block may be the anesthetic of choice for delivery Few cases are encountered in which cyclopropane or combinations of ethylene or nitrous oxide with thiopental cannot be used, however Chloroform, vinyl ether and trichlorethylene are not used because of the possible hepatotoxic effects The muscle relaxants are avoided whenever liver and renal insufficiency exist because these drugs are detoxified by the liver or eliminated by the kidneys

The management of patients with nephritis and other diseases causing impairment of renal function has been discussed in Part II In general the management for obstetric cases presenting renal complications is as outlined in that section Anesthetics which elevate blood pressure, obviously, are avoided as are those which suppress renal function The use of non-volatile drugs should be limited as much as possible Cyclopropane may be used in most instances Ethylene or nitrous oxide may be used for uncomplicated deliveries if administration without anoxia is assured, otherwise ether must be added Until further data is available concerning its effect on the diseased kidney, trichlorethylene is best avoided Chloroform is not used for patients who have renal involvement The various forms of regional anesthesia are preferred to general anesthesia and should be used whenever possible Pudendal, saddle or caudal block are suitable for these patients

Obstetrical patients who have heart disease tuberculosis and other medical complications are managed as outlined in Part II under the various medical complications

## Prematurity

The selection of obstetric analgesia and anesthesia when the birth of a premature infant is anticipated cannot be made by any rule of the thumb Various maternal and obstetrical factors influence the choice If one disregards the maternal and obstetrical factors and considers the problem from the aspect of

the child only, it is obvious that exclusion of all drugs would be the most desirable course to follow However, delivery without anesthesia is not always feasible As a second choice, then, block anesthesia—pudendal, caudal, or saddle block is the most desirable for vaginal delivery Infiltration or spinal block are most desirable for Caesarean section Maternal and obstetrical factors may preclude the use of these, in which case, general anesthesia must be selected The volatile drugs, by virtue of their mode of elimination, are the most desirable, and of these, the gases are the primary choice because they are eliminated most rapidly Nitrous oxide or ethylene would be the most desirable if they could be used in non asphyxial concentrations, but, they cannot, unless used in combination with non volatile drugs This, of course, is not desired Cyclopropane has much to offer because it is labile, rapid acting, eliminated quickly, it permits any desired depth of anesthesia and adequate oxygenation is always assured The volatile liquids are not eliminated as quickly and are, therefore, less desirable Besides, some are cardiotoxic or hepatotoxic The non volatile drugs such as the barbiturates and the narcotics all contribute to respiratory depression and, therefore, should not be used

## REFERENCES

ADRIANI, JOHN *Current Therapy* Philadelphia, Saunders 1954
BROWN J M, VOLPITTO, P P and TORPIN R Anesthesia during labor *Anesthesiology, 10* 15-20 1949
GORDON, R A MORTON, M V Trichlorethylene in obstetric anesthesia and analgesia *Anesthesiology, 12* 680-687, 1951
GREENHILL J P *Analgesia and Anesthesia for Obstetrics* Springfield Thomas 1952
HERSHENSON, B B Premedication and anesthesia in obstetrics *Anesthesiology, 9* 73-85, 1948
HINGSON R, HELLMAN L Organization of an obstetric anesthesia service *Anesthesiology 12* 745-754 1951
LUND P C Role of conduction anesthesia in the management of eclampsia *Anesthesiology 12* 693-705 1951

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*This Book*

# Selection of Anesthesia

*By* John Adriani, M D

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